

From: Swope, Sheridan  
 Sent: Saturday, December 04, 2004 5:25 PM  
 To: Schreiber, David  
 Subject: FW: 09/940,235

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David Dearest,

Would you do the following alignments for me?

From 09/940,235:

Align SID 4, residues 1-106 with each of the sequences below:

Align SID 4, residues 150-259 with each of the sequences below:

✓ 1-106 ✓ 150-259 THANK YOU VERY MUCH!!  
 ✓ Pending Data Base  
 ✓ PCT/US93/09502: SID 1  
 ✓ US08/128,299: SID 1  
 ✓ A\_Geneseq Data Base  
 ✓ AAR10194  
 ✓ AAR63120  
 ✓ AAY24794  
 ✓ AAW94664  
 ✓ AAY01556  
 ✓ AAY24797  
 ✓ UniProt\_02 Data Base  
 ✓ STRP\_STREQ  
 ✓ Issued Patents Data Base  
 ✓ US 09/211,542: SID 6 ✓ 4/1  
 ✓ US 07/549,049 (US 5,240,845) SID 1 & SID 2 & SID 3 ← no biotech data  
 ✓ JS 08/560,098: SID 52 X  
 ✓ US 09/211,542: SID 2 & SID 5 X → NA  
 ✓ US 08/568,393B: ↑ SID 1  
 ✓ GenEmbl Data Base  
 ✓ E03308  
 ✓ AR143998  
 ✓ STRSKC  
 ✓ SEDEXB  
 ✓ J05204  
 ✓ AA  
 ✓ N\_GeneSeq Data Base  
 ✓ AAX80492  
 ✓ AAX16632  
 ✓ AAX80497

Result No.	Score	Query Match	Length	DB ID	Description	Summaries
1	45	7.5	1262	2 E03308 ] 1	ACCESSION: E03308 ACCESSION: K02986 ACCESSION: X78325 ACCESSION: E03308 ACCESSION: AR43998 ACCESSION: AR43998 Streptokinase and Streptokinase and ACCESSION: X78325 Streptococcus equi Streptococcus equi	Alignment Scores: Pred. No.: 0-651 Score: 45.00 Percent Similarity: 42.96% Best Local Similarity: 28.57% Query Match: 7.50% DB: 2 Length: 1262 Matches: 22 Conservative: 11 Mismatch: 21 Indels: 23 Gaps: 6
2	44	7.3	2568	5 STRSKC ] 1	ACCESSION: E03308 ACCESSION: K02986 ACCESSION: X78325 ACCESSION: E03308 ACCESSION: AR43998 ACCESSION: AR43998 Streptokinase and Streptokinase and ACCESSION: X78325 Streptococcus equi Streptococcus equi	Alignment Scores: Pred. No.: 0-651 Score: 45.00 Percent Similarity: 42.96% Best Local Similarity: 28.57% Query Match: 7.50% DB: 2 Length: 1262 Matches: 22 Conservative: 11 Mismatch: 21 Indels: 23 Gaps: 6
c 4	43	7.2	1262	1 AR43998 ] 1	ACCESSION: E03308 ACCESSION: AR43998 ACCESSION: AR43998 Streptokinase and Streptokinase and ACCESSION: X78325 Streptococcus equi Streptococcus equi	Alignment Scores: Pred. No.: 0-651 Score: 45.00 Percent Similarity: 42.96% Best Local Similarity: 28.57% Query Match: 7.50% DB: 2 Length: 1262 Matches: 22 Conservative: 11 Mismatch: 21 Indels: 23 Gaps: 6
c 5	38	6.3	2385	1 AR43998 ] 1	ACCESSION: E03308 ACCESSION: AR43998 ACCESSION: AR43998 Streptokinase and Streptokinase and ACCESSION: X78325 Streptococcus equi Streptococcus equi	Alignment Scores: Pred. No.: 0-651 Score: 45.00 Percent Similarity: 42.96% Best Local Similarity: 28.57% Query Match: 7.50% DB: 2 Length: 1262 Matches: 22 Conservative: 11 Mismatch: 21 Indels: 23 Gaps: 6
c 6	38	6.3	2385	8 AAX60497 ] 1	ACCESSION: E03308 ACCESSION: AR43998 ACCESSION: AR43998 Streptokinase and Streptokinase and ACCESSION: X78325 Streptococcus equi Streptococcus equi	Alignment Scores: Pred. No.: 0-651 Score: 45.00 Percent Similarity: 42.96% Best Local Similarity: 28.57% Query Match: 7.50% DB: 2 Length: 1262 Matches: 22 Conservative: 11 Mismatch: 21 Indels: 23 Gaps: 6
c 7	38	6.3	2385	8 AAX60497 ] 1	ACCESSION: E03308 ACCESSION: AR43998 ACCESSION: AR43998 Streptokinase and Streptokinase and ACCESSION: X78325 Streptococcus equi Streptococcus equi	Alignment Scores: Pred. No.: 0-651 Score: 45.00 Percent Similarity: 42.96% Best Local Similarity: 28.57% Query Match: 7.50% DB: 2 Length: 1262 Matches: 22 Conservative: 11 Mismatch: 21 Indels: 23 Gaps: 6
c 8	38	6.3	2385	8 AAX60497 ] 1	ACCESSION: E03308 ACCESSION: AR43998 ACCESSION: AR43998 Streptokinase and Streptokinase and ACCESSION: X78325 Streptococcus equi Streptococcus equi	Alignment Scores: Pred. No.: 0-651 Score: 45.00 Percent Similarity: 42.96% Best Local Similarity: 28.57% Query Match: 7.50% DB: 2 Length: 1262 Matches: 22 Conservative: 11 Mismatch: 21 Indels: 23 Gaps: 6
c 9	38	6.3	8931	4 SEDDXB ] 1	ACCESSION: E03308 ACCESSION: AR43998 ACCESSION: AR43998 Streptokinase and Streptokinase and ACCESSION: X78325 Streptococcus equi Streptococcus equi	Alignment Scores: Pred. No.: 0-651 Score: 45.00 Percent Similarity: 42.96% Best Local Similarity: 28.57% Query Match: 7.50% DB: 2 Length: 1262 Matches: 22 Conservative: 11 Mismatch: 21 Indels: 23 Gaps: 6
c 10	33.5	5.6	1242	6 AAX6632 ] 1	ACCESSION: E03308 ACCESSION: AR43998 ACCESSION: AR43998 Streptokinase and Streptokinase and ACCESSION: X78325 Streptococcus equi Streptococcus equi	Alignment Scores: Pred. No.: 0-651 Score: 45.00 Percent Similarity: 42.96% Best Local Similarity: 28.57% Query Match: 7.50% DB: 2 Length: 1262 Matches: 22 Conservative: 11 Mismatch: 21 Indels: 23 Gaps: 6
c 11	33.5	5.6	1242	7 AAX60492 ] 1	ACCESSION: E03308 ACCESSION: AR43998 ACCESSION: AR43998 Streptokinase and Streptokinase and ACCESSION: X78325 Streptococcus equi Streptococcus equi	Alignment Scores: Pred. No.: 0-651 Score: 45.00 Percent Similarity: 42.96% Best Local Similarity: 28.57% Query Match: 7.50% DB: 2 Length: 1262 Matches: 22 Conservative: 11 Mismatch: 21 Indels: 23 Gaps: 6
Run on: December 6, 2004, 15:00:52 ; Search time 2 Seconds (without alignments) 2.533 Million cell updates/sec						
Title: US-09-940-235-4						
Perfect score: 600						
Sequence: 1 QAOQMVPQSPVAVSQSKPG.....SMIWDTCTCIGAGRGRISCTI 106						
Scoring table: BLOSUM62						
Xgapop 10.0 ; Xgapext 0.5						
Ygapop 10.0 ; Ygapext 0.5						
Fgapop 6.0 ; Fgapext 7.0						
Delop 6.0 ; Delext 7.0						
Searched: 10 seqs, 23900 residues						
Total number of hits satisfying chosen parameters: 20						
Minimum DB seq length: 0						
Maximum DB seq length: 2000000000						
Post-processing: Minimum Match 0% Maximum Match 100% Listing First 20 summaries						
Command line parameters: -MODEL=frame+_D2n.model -DEV=soft -Q=Pending Patents AA Main US-09-940-235-4 -DB= * -SUFFIX= -pco -OUT=align4_1_106_seq -MINMATCH=0.7 -LOOPEXT=0 -UNITS=bits -START=1 -END=406 -MATRIX=blosum62 -TRANS=human40_cdi -LIST=20 -DOCALIGN=100 -THR SCORE=0CT -THR MAX=100 -THR MIN=0 -ALIGN=20 -MODE=LOCAL -OUTFILE=ptc -NORM=ext -HEAPSIZE=500 -MINLEN=0 -MAXLEN=2000000 -NCPU=6 -NO_XLPPX -NEG SCORES=0 -HEAPSIZE=500 -NTHREADS=1 -XGAPOP=10 -XGAPET=0.5 -FGAPOP=6 -FGAPEXT=7 -YGAPOP=10 -YGAPEXT=0.5 -DELPOP=6 -DELEXT=7						
Database : * : * 1: /staff_overflow/sdavid-tmp/deco4/bwope235/seq/ar143998_gb_pat: * 2: /staff_overflow/sdavid-tmp/deco4/bwope235/seq/e03308_gb_pat: * 3: /staff_overflow/sdavid-tmp/deco4/bwope235/seq/i05204_gb_pat: * 4: /staff_overflow/sdavid-tmp/deco4/bwope235/seq/sedexb_gb_pat: * 5: /staff_overflow/sdavid-tmp/deco4/bwope235/seq/strskc_gb_pat: * 6: /staff_overflow/sdavid-tmp/deco4/bwope235/seq/aaX60497_gb_pat: * 7: /staff_overflow/sdavid-tmp/deco4/bwope235/seq/aaX6632_gb_pat: * 8: /staff_overflow/sdavid-tmp/deco4/bwope235/seq/aaX80492_gb_pat: * 9: /staff_overflow/sdavid-tmp/deco4/bwope235/seq/us-09-211-342a-: * 10: /staff_overflow/sdavid-tmp/deco4/bwope235/seq/us-09-568-393b-1: *						
Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.						
Summaries						
Result No.	Score	Query Match	Length	DB ID	Description	Summaries
1	45	7.5	1262	2 E03308 ] 1	ACCESSION: E03308 ACCESSION: K02986 ACCESSION: X78325 ACCESSION: E03308 ACCESSION: AR43998 ACCESSION: AR43998 Streptokinase and Streptokinase and ACCESSION: X78325 Streptococcus equi Streptococcus equi	Alignment Scores: Pred. No.: 0-651 Score: 45.00 Percent Similarity: 42.96% Best Local Similarity: 28.57% Query Match: 7.50% DB: 2 Length: 1262 Matches: 22 Conservative: 11 Mismatch: 21 Indels: 23 Gaps: 6
2	44	7.3	2568	5 STRSKC ] 1	ACCESSION: E03308 ACCESSION: K02986 ACCESSION: X78325 ACCESSION: E03308 ACCESSION: AR43998 ACCESSION: AR43998 Streptokinase and Streptokinase and ACCESSION: X78325 Streptococcus equi Streptococcus equi	Alignment Scores: Pred. No.: 0-651 Score: 45.00 Percent Similarity: 42.96% Best Local Similarity: 28.57% Query Match: 7.50% DB: 2 Length: 1262 Matches: 22 Conservative: 11 Mismatch: 21 Indels: 23 Gaps: 6
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c 5	38	6.3	2385	1 AR43998 ] 1	ACCESSION: E03308 ACCESSION: AR43998 ACCESSION: AR43998 Streptokinase and Streptokinase and ACCESSION: X78325 Streptococcus equi Streptococcus equi	Alignment Scores: Pred. No.: 0-651 Score: 45.00 Percent Similarity: 42.96% Best Local Similarity: 28.57% Query Match: 7.50% DB: 2 Length: 1262 Matches: 22 Conservative: 11 Mismatch: 21 Indels: 23 Gaps: 6
c 6	38	6.3	2385	8 AAX60497 ] 1	ACCESSION: E03308 ACCESSION: AR43998 ACCESSION: AR43998 Streptokinase and Streptokinase and ACCESSION: X78325 Streptococcus equi Streptococcus equi	Alignment Scores: Pred. No.: 0-651 Score: 45.00 Percent Similarity: 42.96% Best Local Similarity: 28.57% Query Match: 7.50% DB: 2 Length: 1262 Matches: 22 Conservative: 11 Mismatch: 21 Indels: 23 Gaps: 6
c 7	38	6.3	2385	8 AAX60497 ] 1	ACCESSION: E03308 ACCESSION: AR43998 ACCESSION: AR43998 Streptokinase and Streptokinase and ACCESSION: X78325 Streptococcus equi Streptococcus equi	Alignment Scores: Pred. No.: 0-651 Score: 45.00 Percent Similarity: 42.96% Best Local Similarity: 28.57% Query Match: 7.50% DB: 2 Length: 1262 Matches: 22 Conservative: 11 Mismatch: 21 Indels: 23 Gaps: 6
c 8	38	6.3	8931	4 SEDDXB ] 1	ACCESSION: E03308 ACCESSION: AR43998 ACCESSION: AR43998 Streptokinase and Streptokinase and ACCESSION: X78325 Streptococcus equi Streptococcus equi	Alignment Scores: Pred. No.: 0-651 Score: 45.00 Percent Similarity: 42.96% Best Local Similarity: 28.57% Query Match: 7.50% DB: 2 Length: 1262 Matches: 22 Conservative: 11 Mismatch: 21 Indels: 23 Gaps: 6
c 9	38	6.3	8931	4 SEDDXB ] 1	ACCESSION: E03308 ACCESSION: AR43998 ACCESSION: AR43998 Streptokinase and Streptokinase and ACCESSION: X78325 Streptococcus equi Streptococcus equi	Alignment Scores: Pred. No.: 0-651 Score: 45.00 Percent Similarity: 42.96% Best Local Similarity: 28.57% Query Match: 7.50% DB: 2 Length: 1262 Matches: 22 Conservative: 11 Mismatch: 21 Indels: 23 Gaps: 6
c 10	33.5	5.6	1242	6 AAX6632 ] 1	ACCESSION: E03308 ACCESSION: AR43998 ACCESSION: AR43998 Streptokinase and Streptokinase and ACCESSION: X78325 Streptococcus equi Streptococcus equi	Alignment Scores: Pred. No.: 0-651 Score: 45.00 Percent Similarity: 42.96% Best Local Similarity: 28.57% Query Match: 7.50% DB: 2 Length: 1262 Matches: 22 Conservative: 11 Mismatch: 21 Indels: 23 Gaps: 6
c 11	33.5	5.6	1242	7 AAX60492 ] 1	ACCESSION: E03308 ACCESSION: AR43998 ACCESSION: AR43998 Streptokinase and Streptokinase and ACCESSION: X78325 Streptococcus equi Streptococcus equi	Alignment Scores: Pred. No.: 0-651 Score: 45.00 Percent Similarity: 42.96% Best Local Similarity: 28.57% Query Match: 7.50% DB: 2 Length: 1262 Matches: 22 Conservative: 11 Mismatch: 21 Indels: 23 Gaps: 6

Db 992 GTACGACCCGGTGTAACTGGTACACAA-----CTTGATGCTT--- 1042 Best Local Similarity: 23.81% Mismatches: 14 DB: 7.33% Indels: 10 Gaps: 5

Qy 24 AsnGlyIysHistYrgInIleAsnGlnGlnTrp-----Gluarg-ThrTyrlieuGlyAs 41 Query Match: STRSKC (1-256)

Db 1043 -----CGTATCATGGACTACACCCGTACTGGTAAAGTAGACACATGAGCAC 1096 Qy 2 AlaGlnGlnMetValGlnProGlnSerProValAlaValSerGlnSerIysProGlyCys 21 DB: 3.19 GCAAGACCTCTATGACCCACCTCAAGTAAAGCTCTT----- 366

Qy 41 nValLeuValCysThrCysTrGlyGlySerAsnGlyPheAsnCysGluSerLysProG 61 Qy 22 TyrAspArgGlyIysHistYrgInIleAsnGlnGlnTrpGluArgThrTyrLeuGlyAsn 41 DB: 3.67 -----TTTCGATATACATGATTGGAAAATGACATATGGTCCC 408

Db 1097 CAACCGTATCATGACCGTATCATGGCAAACTGGATATGACAAAGCGTACAC 1135 Qy 42 ValLeu 43

Db 1136 AGGTGAAATGATGATCTTACATCTGGATATGACAAAGCGTACAC 1184 Qy 409 CTCCTT 414

RESULT 2

STRSKC LOCUS Streptococcus equisimilis (H46A) streptokinase gene, complete cds. RESULT 3

DEFINITION BCT 26-APR-1993 SBDXB

ACCESSION K02886.1 GI:153808 LOCUS SEDEXB

VERSION X72832.1 GI:407876 DEFINITION S. equisimilis dexb, abc, lrp, skc, rel genes and ORF1.

KEYWORDS Streptokinase, dsgalactiae subsp. equisimilis ACCESSION X72832

SOURCE Streptococcus dsgalactiae subsp. equisimilis VERSION X72832.1 GI:407876

ORGANISM Bacteria: Firmicutes; Lactobacillales; Streptococcaceae; KEYWORDS abc gene; ABC transporter; dexB gene; dextran glucosidase; glucan 1,6-alpha-D-glucosidase; leucine rich protein; LRP gene; ORF1; rel gene; skc gene; streptokinase; stringent response-like protein.

REFERENCE 1 (bases 1 to 2568) SOURCE Streptococcus dsgalactiae subsp. equisimilis

AUTHORS Malke, H., Roe, B., and Ferretti, J.J. ORGANISM Bacteria; Firmicutes; Lactobacillales; Streptococcaceae; TITLE Nucleotide sequence of the streptokinase gene from Streptococcus

JOURNAL Gene 34 (2-3), 357-362 (1985) REFERENCE 1 (bases 3621 to 6190)

MEDLINE 85232082 AUTHORS Malke, H., Roe, B., and Ferretti, J.J.

PUBMED 2989113 TITLE Nucleotide sequence of the streptokinase gene from Streptococcus

COMMENT Original source text: *S. equisimilis* (strain H46A) DNA, clone pMFS. J.J. Ferretti, 03-SEP-1985. JOURNAL Gene 34 (2-3), 357-362 (1985)

The -35 and -10 regions are located at positions 760-765 and 781-786 respectively and an SD sequence at 808-813. Downstream from the coding region inverted repeats (positions 2176-2190 and 2203-2217) are thought to function as transcription terminators. The nucleotide sequence of skc does not support the hypothesis that the gene has evolved by duplication and fusion, as suggested by internal two-fold AA homologies of its product.

FEATURES Location/Qualifiers 1..2568

source /organism="Streptococcus dsgalactiae subsp. equisimilis"

/mol\_type="Genomic DNA"

/db\_xref="taxon:119602"

mRNA /product="skc mRNA"

CDS /note="presstreptokinase"

/codon\_start=1

/transl\_table=11

/protein\_id="AAA26974.1"

/db\_xref="GI:157809"

/translation="MKNYLGFGMFALLFALTFGTGTVNSVOAAGPEWLLDRPSVANSOLVVSAGTVEGSTNQDISLKEFPIIDTSRPAIGCGKTEQGLSKSKPAPDSAMSHLEKADLLKAIQKBLIYHNSDDFELVIDFASDITDNGKVFADKGDSVTLTQVQBFLLSGHVRPVYKEPIQNOAQSVDYETVQTFPLNPDDDFRPGIKDTKLKLAIQDTITTSOELLQAOQSILANKHFGTYTVERDSSVTHNDIDFEPILPMDQEFYVQVNREQAYRINKSGSNEEINNTLISKEVYVLLKGEBKPYDODFDRSHLKLFIKVYDINELLKSEQULLTASRNLDLFRDLYDPRDKAGLLVNLDAIGMDTLYGKEDNHDNTNLITVYMGKRGPEGENASVHAYDQRTYEEREVYSLRYTGTPIPNDNDK"

sig\_peptide 819 .. 896 Length: 2568

mat\_peptide 897 .. 2138 Matches: 10

/product="streptokinase signal peptide" Conservative: 8

CDS /note="hairpin loop"

/gene="dexB"

/EC\_number="3.2.1.70"

/codon\_start=1

/transl\_table=11

Alignment Scores:

Pred. No.: 2.05

Score: 44.00

Percent Similarity: 42.86%



/db\_xref="GOA:Q54089"

Alignment Scores:  
 Pred. No.: 8.55 Length: 8931  
 Score: 44.00 Matches: 10  
 Percent Similarity: 42.86% Conservative: 8  
 Best Local Similarity: 23.81% Mismatches: 14  
 Query Match: 7.33% Indels: 10  
 DB: 4 Gaps: 1

US-09-940-235-4 (1-259) x SEDEXB (1-8931)

Qy 2 AlaGlnGlnMetValGlnProGlnSerProValAlaValSerGlnSerIysProGlyCys 21  
 Db 3939 GCGAGCTCATATGGCAACCCCAACTCAAGTAATAAGCCCTCTT----- 3986

Qy 22 TyrAspAsnGlyLysIstYrGlnIleLeuGlnGlnIleGlnIleGlnIleGlnIle 41  
 Db 3987 -----TTTCGGATATAACATGATTGGAAATGCAATATTGGTCCC 4028

Qy 42 ValLeu 43

Db 4029 CTCCT 4034

RESULT 4  
 LOCUS E03308 1262 bp DNA linear PAT 29-SEP-1997  
 DEFINITION DNA encoding recombinant streptokinase.  
 ACCESSION E03308  
 VERSION E03308.1 GI:2171525  
 KEYWORDS JP 1992011892-A/1.  
 SOURCE  
 ORGANISM  
 REFERENCE 1 (bases 1 to 1262)  
 AUTHORS Fujii,S., Katano,T., Majima,E., Ogino,K., Ono,K., Sakata,Y. and Uenoyama,T.  
 TITLE PROTEIN OF STREPTOKINASES, CORRESPONDING GENE, CORRESPONDING PLASMID RECOMBINANT, CORRESPONDING CHARACTER TRANSFORMANT AND PRODUCTION  
 JOURNAL OTSUKA PHARMACEUT FACTORY INC  
 COMMENT OS Artificial gene  
 OS Artificial sequence; Genes.  
 PN JP 1992011892-A/1  
 PD 16-JAN-1992  
 PF 06-JUL-1990 JP 1990179851  
 PR 11-JUL-1989 JP 89P 1794312, 27-NOV-1989 JP 89P 307957, PR 11-APR-1990 JP 90P 96830  
 PI FUJII, SETSUO, KATANO, TAMITAKA, MAJIMA EIJI, OGINO KOICHI, PI  
 ONO KENJI, PI  
 SAKATA, YASUYO, UENOYAMA TSUTOMU  
 PC C12N15/58, C12N1/21, C12N9/70, (C12N1/21, C12R1:19), (C12N9/70, PC C12R1:19);  
 CC strandedness: Double;  
 CC topology: Linear;  
 CC hypothetical: No;  
 CC anti-sense: No;  
 CC \*source: clone=psKR;  
 FH Key  
 FH Location/Qualifiers  
 FT 5' UTR 1. .11  
 FT CDS 12. .1256  
 FT /product=' recombinant streptokinase' FT  
 mat\_peptide 12. .1253  
 FT /product=' recombinant streptokinase' FT  
 3' UTR 1257. .1263  
 FEATURES source  
 /organism="synthetic construct"  
 /mol\_type="genomic DNA"  
 /db\_xref="taxon:32630"

Alignment Scores:  
 Pred. No.: 1.06 Length: 1262  
 Score: 43.00 Matches: 12  
 Percent Similarity: 40.30% Conservative: 15  
 Best Local Similarity: 40.11% Mismatches: 26  
 Query Match: 7.17% Indels: 14  
 DB: 2 Gaps: 1

US-09-940-235-4 (1-259) x E03308 (1-1262)

Qy 36 ArgThrTyrLeuGlyAsnValLeuValCysThrCysSerGlyGlySerArgGlyPheAsn 55  
 Db 293 AGATGTAAGCTTAGGATCAGCTGTTCCCTGGATATGCTT----- 255

Qy 56 CysGluSerIysProGluAlaGluLuthrCysSerAspIleTrpAspCysThrCysThrYrTyr 75  
 Db 254 -----CAGGAGATCTGCCTCTGAGTTATGAGACATAGCGCC 216

Qy 76 ArgValGlyAspThrTyrGluArgProIysAspSerMetIleTrpAspCysThrCysThrIle 95  
 Db 215 AGAGCAGTAGCGAACGGTTAGATTTCGGGAGAGGCCCTGGTTACACCATG 156

Qy 96 GlyAlaGlyArgGlyArgIle 102  
 Db 155 GGGCGACGAGAGGGTCAGGTC 135

RESULT 5  
 LOCUS AR143998 2385 bp DNA linear PAT 08-AUG-2001  
 DEFINITION Sequence 1 from patent US 6210667.  
 ACCESSION AR143998  
 VERSION AR143998.1 GI:15105665  
 KEYWORDS  
 SOURCE Unknown.  
 ORGANISM Unclassified.  
 REFERENCE 1 (bases 1 to 2385)  
 AUTHORS Reed,G.L.  
 TITLE Bacterial fibrin-dependent plasminogen activator  
 JOURNAL Patent: US 6210667-A 1 03-APR-2001;  
 FEATURES Location/Qualifiers  
 source 1. .2385  
 /organism="unknown"  
 /mol\_type="unassigned DNA"

Alignment Scores:  
 Pred. No.: 7.15 Length: 2385  
 Score: 38.00 Matches: 15  
 Percent Similarity: 33.90% Conservative: 5  
 Best Local Similarity: 25.12% Mismatches: 35  
 Query Match: 6.33% Indels: 4  
 DB: 1 Gaps: 1

US-09-940-235-4 (1-259) x AR143998 (1-2385)

Qy 14 ValSerGlnSerIysProGlyCysThrCysAspGlyLysIstYrGlnIleAsnGlnGln 33  
 Db 933 GTTGGGAAAGATCCACGTTAGCCACCATGAAACGCCAAGAAAGGTGAATCAT 992

Qy 34 TrpGluArgThrTyrLeuGlyAsnValIeuaIysThrCysThrGlyIle----- 50  
 Db 993 GCCGAACATCCGAGATGTCGTTCTGGTATGCCGTGATAAACGC 1052

RESULT 6  
 LOCUS AR143998\_c  
 DEFINITION Sequence 1 from patent US 6210667.  
 ACCESSION AR143998  
 VERSION AR143998.1 GI:15105665

KEYWORDS SOURCE Unknown.  
ORGANISM Unknown.  
Unclassified.  
1 (bases 1 to 2385)

REFERENCE Reed, G.L.  
AUTHORS Reed, G.L.  
TITLE Bacterial fibrin-dependent plasminogen activator  
JOURNAL Patent: US 6210667, A1 03-APR-2001;  
FEATURES Location,Qualifiers  
Source  
1..2385  
/mol\_type="unknown"  
/mol\_type="unassigned DNA"

Alignment Scores:  
Pred. No.: 7.15 Length: 2385  
Score: 38.00 Matches: 11  
Percent Similarity: 38.89% Conservative: 3  
Best Local Similarity: 30.56% Mismatches: 22  
Query Match: 6.33% Indels: 0  
DB: 0 Gaps: 0

US-09-940-235-4 (1-259) x ARI13998 (1-2385)  
Qy 1 GlnAlaGlnGlnMetValGlnSerProValAlaValSerGlnSerProGly 20  
Db 1156 CAGGTCAGCATCTTACCTCTGATGGATCCGGCGGGTACCGAGCTGAATTAGTC 1097

Qy 21 CyBtYtAspAlaGlyLysHistYtrglnLysGlnTrpGluLys 36  
Db 1096 CGCGTCCTTCAGGCTTCATGACAGTCAGACATGACACTGACGACCTGGCCCT 1049

RESULT 7  
AAX80497 standard; cDNA: 2385 BP.  
ID AAX80497  
AC AAX80497;  
XX DT 26-AUG-1999 (first entry)  
XX Streptokinase and maltose binding protein fusion protein encoding cDNA.  
KW Streptococcus; streptokinase; fibrin-dependent plasminogen activator;  
KW rSK; bacterial; blood clot; thrombotic condition;  
KW myocardial infarction; venous thrombosis; pulmonary embolism;  
KW cerebral thrombosis; graft thrombosis; arterial thrombosis; ss.  
XX Streptokinase and maltose binding protein fusion protein encoding cDNA.  
OS Synthetic.  
XX PN W0931247-A1.  
XX PD 24-JUN-1999.  
XX PT 15-DEC-1998; 98WO-US026694.  
XX PR 15-DEC-1997; 97US-0069497P.  
XX PA (HARD ) HARVARD COLLEGE.  
PI Reed GL;  
XX DR 1999-395183/33.  
XX PT N-terminally deleted streptokinase.  
XX Example: Page 45-48; 73pp; English.  
XX The present invention describes an isolated bacterial protein that  
CC induces Fibrin-dependent plasminogen activation in a pharmaceutical  
CC composition for dissolving blood clots. Also described are: (1) a  
CC composition comprising an isolated modified streptokinase, the  
CC modification being removal of amino acid residues in the amino terminus;

CC (2) a method for dissolving a blood clot in a subject, comprising  
CC administering to the subject a fibrin-dependent streptokinase protein; a  
CC nucleic acid (1) encoding a modified bacterial streptokinase; (3) an  
CC expression vector comprising (1); and (4) a host cell transformed with  
CC the expression vector of (3). The pharmaceutical composition comprising  
CC bacterial fibrin-dependent plasminogen activator is useful for dissolving  
CC blood clots in patients with a thrombotic condition, e.g. myocardial  
CC infarction, venous thrombosis, pulmonary embolism, cerebral thrombosis,  
CC graft thrombosis and arterial thrombosis. The modified streptokinase can  
CC also be used in non-human mammals. Streptokinase activation of  
CC plasminogen is at least 10-fold greater in the presence of fibrin. The modified  
CC streptokinase has at least one amino acid substitution that inactivates a  
CC substrate site for proteolytic cleavage. This reduces the rate of  
CC degradation of the streptokinase at least two-fold. The present sequence  
CC encodes a streptokinase and maltose binding protein fusion protein from  
CC an example of the present invention  
XX SQ Sequence 2385 BP; 745 A; 547 C; 544 G; 544 T; 0 U; 0 Other;

Alignment Scores:  
Pred. No.: 7.15 Length: 2385  
Score: 38.00 Matches: 15  
Percent Similarity: 33.90% Conservative: 5  
Best Local Similarity: 25.42% Mismatches: 35  
Query Match: 6.33% Indels: 4  
DB: 8 Gaps: 1

US-09-940-235-4 (1-259) x AAX80497 (1-2385)  
Qy 14 ValSerGlnSerLysProGlyCystYtAspAsnGlyLysHistYtrglnIleAsnGlnGln 33  
Db 933 GtttGCGAAAGATTCACCTATGCGCACCATGGAAACGCCAGAAAGGTGAATAT 992

Qy 34 TrpGluArgThrTyrLeuGlyAsnValLeuValCysThrCysTrpGlyGly---- 50  
Db 993 GCGGAACATCCCGCAGATGTCGCTTCTGGPATGCCGTGCTACTGGGTGATCAAACGC 1052

Qy 51 ---SerArgGlyPheAsnCysGluSerLysProGluAlaLglLglLthCysPheAEP 68  
Db 1053 CGCCAGCGGTCTGTCATGACACTGACATGACGACCTGGCCCTGAAGACGCCAGACTAATTGAG 1109

RESULT 8  
AAX80497/C  
ID AAX80497 standard; cDNA: 2385 BP.  
XX AC AAX80497;  
XX DT 26-AUG-1999 (first entry)  
XX Streptokinase and maltose binding protein fusion protein encoding cDNA.  
XX Streptococcus; streptokinase; fibrin-dependent plasminogen activator;  
XX rSK; bacterial; blood clot; thrombotic condition;  
XX myocardial infarction; venous thrombosis; pulmonary embolism;  
XX cerebral thrombosis; graft thrombosis; arterial thrombosis; ss.  
XX Streptococcus dysgalactiae subsp. equisimilis.  
OS Synthetic.  
XX PN W0931247-A1.  
XX PD 24-JUN-1999.  
XX PT 15-DEC-1998; 98WO-US026694.  
XX PR 15-DEC-1997; 97US-0069497P.  
XX PA (HARD ) HARVARD COLLEGE.  
PI Reed GL;  
XX DR P-PSDB; AAY24797.  
XX PT N-terminally deleted streptokinase.  
XX Example: Page 45-48; 73pp; English.  
XX The present invention describes an isolated bacterial protein that  
CC induces Fibrin-dependent plasminogen activation in a pharmaceutical  
CC composition for dissolving blood clots. Also described are: (1) a  
CC composition comprising an isolated modified streptokinase, the  
CC modification being removal of amino acid residues in the amino terminus;

CC Streptokinase and maltose binding protein fusion protein encoding cDNA.  
XX KW Streptococcus; streptokinase; fibrin-dependent plasminogen activator;  
KW rSK; bacterial; blood clot; thrombotic condition;  
KW myocardial infarction; venous thrombosis; pulmonary embolism;  
KW cerebral thrombosis; graft thrombosis; arterial thrombosis; ss.  
XX Streptococcus dysgalactiae subsp. equisimilis.  
OS Synthetic.  
XX PN W0931247-A1.  
XX PD 24-JUN-1999.  
XX PT 15-DEC-1998; 98WO-US026694.  
XX PR 15-DEC-1997; 97US-0069497P.  
XX PA (HARD ) HARVARD COLLEGE.  
PI Reed GL;  
XX DR WPI; 1999-395183/33.

DR	P-PSDB; AAY24797.	JOURNAL	Mol. Gen. Genet. 241 (1-2), 129-140 (1993)
XX	N-terminally deleted streptokinase.	JOURNAL	
XX	Example; Page 45-48; 73pp; English.	REFERENCE	3 (bases 1 to 8931)
PS		AUTHORS	Malke, H.
XX	The present invention describes an isolated bacterial protein that induces fibrin-dependent plasminogen activation in a pharmaceutical composition comprising for dissolving blood clots. Also described are: (1) a composition comprising an isolated modified streptokinase, the modification being removal of amino acid residues in the amino terminus; (2) a method for dissolving a blood clot in a subject, comprising administering to the subject a fibrin-dependent streptokinase protein; (3) an nucleic acid (1) encoding a modified bacterial streptokinase; (4) a host cell transformed with the expression vector comprising (1); and (5) a host cell transformed with the expression vector of (3). The pharmaceutical composition comprising a bacterial fibrin-dependent plasminogen activator is useful for dissolving blood clots in patients with a thrombotic condition, e.g. myocardial infarction, venous thrombosis, pulmonary embolism, cerebral thrombosis, graft thrombosis and arterial thrombosis. The modified streptokinase can also be used in non-human mammals. Streptokinase activation of plasminogen is at least 10-fold, preferably 100-fold greater in the presence of fibrin than in the absence of fibrin. The modified streptokinase has at least one amino acid substitution that inactivates a substrate site for proteolytic cleavage. This reduces the rate of degradation of the streptokinase at least two-fold. The present invention encodes a streptokinase and maltose binding protein fusion protein from an example of the present invention	JOURNAL	Direct Submission
CC		TITLE	Submitted (05-MAY-1993) H. Malke, Institute for Molecular Biology, Jena University, Winzerller Str 10, 07708 Jena, FRG
CC		COMMENT	Related sequences: K02986, M19346, X13399 & X13400.
CC		FEATURES	Location/Qualifiers
CC		source	1. 8931 /organism="streptococcus dysgalactiae subsp. equisimilis" /mol_type="genomic DNA" /isolate="human group C strain" /strain="H46A" /spec="human group C strain"
CC			/sub _spec="equisimilis"
CC			/db_xref="TAXON:119602"
CC			/chromosome="streptokinase region"
CC			/clone_id="B-coli Plasmid library containing subfragments of the submitted seq:PSHD14/16, PSPV19, PSH2, PMF1, PCWP73, PRH10, PWX4"
CC			/complement(89..1761)
CC			/gene="dexB"
CC			/complement(89..115)
CC			/gene="dexB"
CC			/note="hairpin loop"
CC			/complement(136..1749)
CC			/gene="dexB"
CC			/EC number="3.2.1.70"
CC			/codon_start=1
CC			/transl_table=11
CC			/product="glucan 1,6-alpha-glucosidase"
CC			/protein_id="CAA51348.1"
CC			/db_xref="GI:407877"
CC			/db_xref="GO:Q59905"
CC			/translation="MOKQWNNKATIYQIYPRSFKDTSQNGIGDLRGITSOLDYLRQLG
CC			ITAIWLSPTOSPMDDNGIDSDYEAEVQNMDDMDLIIAANERIKIKIMDLVW
CC			HTSDEIWAHYARENAPNSPDDNGISPEDDYYTWRDEPNLMSLFSWELDEASQYQLHFSK
CC			KOPDINWEAHYRQKLYDMNFWIAKGIGGERMDVIDLIGKLPDSELTGNSQPRHLFYL
CC			KEMNQATQFGNDHMTVQGATPEA1QKSRPENKELQGIGWNSLFWNNHDLPRVLSIWENDSLYREKSAKA
CC			DYAEELDWPALKTIFSRKWTQELKGIGWNSLFWNNHDLPRVLSIWENDSLYREKSAKA
CC			LAILIILHMRGPYIYQEBELGTMNPYKPKDLTEVDDIESLYNAKEAMENGVPAAIMVSS
CC			IRKVGDRNDAPMWSKDTIAGSEQEWTLPNPNVQEINTVADALANQDSIIFYVQO
CC			LIALRKDQWVNEATDYLPTADKVPAYQDQVFAKDLGAE
CC			VVITNTDVKVLETHLQLQPWDAFCVYKLSV"
CC			/complement(1757..1761)
CC			/gene="dexB"
CC			/complement(1780..3051)
CC			/gene="abc"
CC			/complement(1780..1810)
CC			/gene="abc"
CC			/note="hairpin loop"
CC			/complement(2482..2499)
CC			/gene="abc"
CC			/note="Walker motif B"
CC			/complement(2633..2995)
CC			/gene="abc"
CC			/codon_start=1
CC			/transl_table=11
CC			/product="ABC transporter"
CC			/protein_id="CAA51349.1"
CC			/db_xref="GI:600072"
CC			/db_xref="GO:Q54086"
CC			/translation="MVELNLNHA1YKXYPNTHYAYEDFLD1KDEPFTVVFVGPSCGK
CC			STTLRMTAGLDESEGELKIDGEVNDKSPKDRD1AMVQNYALPHMTYVDNMATGL
CC			KLRKFKKR"
CC			/complement(2644)
CC			/gene="abc"
CC			/note="abc"
CC			2 (bases 1 to 4188; 5790 to 8931)
REFERENCE			/db_xref="TREMBL:Q54186"
REFERENCE			/translation="MVELNLNHA1YKXYPNTHYAYEDFLD1KDEPFTVVFVGPSCGK
AUTHORS	Malke, H., Roe, B. and Ferretti, J.J.	JOURNAL	Gene 34 (2-3), 357-362 (1985)
AUTHORS	Mechold, U., Steiner, K., Vettermann, S. and Malke, H.	FEATURE	9
TITLE	Genetic organization of the streptokinase gene from Streptococcus equisimilis H46A	LOCUS	SEDEXB
VERSION	X72832	DEFINITION	S.equisimilis dexb, abc, 1rp, skc, rel genes and ORF1.
KEYWORDS		ACCESSION	X72832.1 GI:407876
SOURCE		VERSION	X72832.1 GI:407876
ORGANISM		STREPTOCOCCUS	streptokinase; leucine rich protein; LRP gene; ORF1; rel gene; skc gene; streptokinase; streptococcus dysgalactiae subsp. equisimilis
REFERENCE	1 (bases 3621 to 6190)	STREPTOCOCCUS	streptococci; Bacteria; Firmicutes; Lactobacillales; Streptococaceae;
AUTHORS	Malke, H., Roe, B. and Ferretti, J.J.	DEFINITION	Streptococcus equisimilis H46A
TITLE	Nucleotide sequence of the streptokinase gene from Streptococcus equisimilis H46A	ACCESSION	Gene 34 (2-3), 357-362 (1985)
JOURNAL		VERSION	85232082
PUBMED	2989113	DEFINITION	2 (bases 1 to 4188; 5790 to 8931)
REFERENCE		ACCESSION	2 (bases 1 to 4188; 5790 to 8931)
AUTHORS	Mechold, U., Steiner, K., Vettermann, S. and Malke, H.	DEFINITION	/note="(+1) frame shift mutation in H46A"
TITLE	Genetic organization of the streptokinase gene from Streptococcus equisimilis H46A	ACCESSION	/complement(2828..2854)
		VERSION	/gene="abc"





US-09-940-235-4 (1-259) x us-09-211-542a-5 (1-1242)	AC AAX16632;
Qy 44 ValCysThrCystyrglySerArgGlySerAsnCysGluSerLysProGluAlaGlu 63	XX DT 17-OCT-2003 (revised)
Db 1090 ATCATAACGTTATATGGCAAGCGA ----- CCGGAGGGAG 1128	XX DT 04-MAY-1999 (first entry)
Qy 64 GluThrCysPhe ----- AspLysTyrThr 71	XX Streptococcus equisimilis native streptokinase encoding DNA.
Db 1129 AATGCTAGCTATCATTTAGCCATTAGCTATGATAAAGATCGTTATACC 1170	KW Streptococcus equisimilis H46A; streptokinase; mutant; fibrinolytic; plasma clot; hydrolysis; haemolytic Streptococcus; plasminogen; plasmin; serine protease; fibrin; blood clot; thrombolytic; vascular thromboembolic symptom; acute myocardial infarction; fibrinolysis; resistance; ds.
RESULT 13 us-08-568-393b-1	XX OS Streptococcus dysgalactiae subsp. equisimilis.
Alignment Scores:	XX Location/Qualifiers
Pred. No. : 8.8	Length: 1242
Score: 33.50	Matches: 10
Percent Similarity: 38.24%	Conservative: 3
Best Local Similarity: 29.41%	Missmatches: 8
Query Match: 5.58%	Indels: 13
DB: 10	Gaps: 2
	XX Key FH
	CDS FT
	/*tag= a
	/transl_except= (pos:40. .42, aa:Asn)
	/note= "no stop codon given"
	XX FT
	XX PN US5876999-A.
	XX XX
	PD 02-MAR-1999.
	PP 06-DEC-1995;
	PR 06-DEC-1995;
	XX 95US-00568393.
	XX 95US-00568393.
	PA (NASC-) NAT SCI COUNCIL.
	XX PI Wu H;
	XX DR WPI: 1999-185643/16.
	DR P-PSDB; AAW94664.
	XX PT Mutant streptokinase polypeptide - useful as plasmin-resistant thrombolytic agent.
	XX XX Claim 1; Col 7-10; 17pp; English.
	XX CC The present invention describes a mutant streptokinase (SK) polypeptide in which at least one of the amino acids in the Pro8-Lys59-Ser60-Lys61 segment of the corresponding native SK is replaced by another amino acid.
	CC The present sequence encodes native SK. SK is a secretory protein of CC haemolytic Streptococcus able to activate human plasminogen (HPlg) to CC plasmin (HPIm), which is a serine protease able to catalyse the CC hydrolysis of fibrin in blood clots. The SK is useful as a thrombolytic CC agent in the treatment of vascular thromboembolic symptoms such as CC acute myocardial infarction. Compared with wild-type SK, the K58 mutant CC is more resistant to degradation by human plasmin and is more effective CC both in acting as a fibrolytic agent and in activating human plasminogen. CC (Updated on 17-OCT-2003 to standardise OS field)
	XX XX
	ORGANISM Unknown.
	UNCLASSIFIED Unclassified.
	REFERENCE 1 (bases 1 to 1401)
	AUTHORS Hagenson, M.J. and Stroman, D.W.
	TITLE Yeast production of streptokinase
	JOURNAL Patent: EP 0248227-A1 5 09-DEC-1987;
	FEATURES Location/Qualifiers
	SOURCE 1..1401
	/organism="unknown"
	/mol_type="unassigned DNA"
	Alignment Scores:
Pred. No. : 9.86	Length: 1401
Score: 33.50	Matches: 10
Percent Similarity: 38.24%	Conservative: 3
Best Local Similarity: 29.41%	Missmatches: 8
Query Match: 5.58%	Indels: 13
DB: 3	Gaps: 2
	XX Pred. No.: 17 4 Length: 1242
	Score: 28.50 Matches: 12
	Percent Similarity: 34.62% Conservative: 6
	Best Local Similarity: 23.08% Mismatches: 19
	Query Match: 4.75% Indels: 15
	DB: 6 Gaps: 2
	Sequence 1242 BP; 423 A; 268 C; 314 T; 0 U; 0 Other;
	XX SQ Alignment Scores:
	XX Pred. No.: 17 4 Length: 1242
	Score: 28.50 Matches: 12
	Percent Similarity: 34.62% Conservative: 6
	Best Local Similarity: 23.08% Mismatches: 19
	Query Match: 4.75% Indels: 15
	DB: 6 Gaps: 2
	US-09-940-235-4 (1-259) x AAX16632 (1-1242)
Qy 64 GluThrCysPhe ----- AspLysTyrThr 71	Qy 5 MetValGlnProGlnSerProVal-----AlaValSerGlnSerLysProGlyCystyr 22
Db 1138 AATGCTAGCTATCATTTAGCCATTAGCTATGATAAAGATCGTTATACC 1179	Db 581 ArgGTCACCGATAAGCTGTTCAATAGCTTAGTATCCTGAGCTGCTGAA 522
RESULT 15	Qy 23 AspGlyLysHistyrglySerArgGlySerAsnCysGluSerLysProGluAlaGlu 63
AAX16632/C	Db 521 TCGTCACTAGGGTTAAAGGAGAAAC----- 495
ID AAX16632 standard; DNA; 1242 BP.	XX



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protein_id="AAZ6974_1"
/db_xref="GI:153609"
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VVSAGRVEGTNQDISLKFEDLTSRAHGGTIEQGUSPKSKPFAOTSGAMSILKE
ADLKAHQEQLJANVHSNDYPAVIFDASATIDTRNCKVFADKDGTSLPTOPVOE
PLISGHVYRPKPEKIQNQKAVSIVTQFPLNBDPDERQBLKDKLFLKTRLAIGD
TITSQELLAQAGSILNKGHPGTIYERDSIVTHNDLFTTLPMDQBTETYVKNREQ
AYRINKKSGSLABINNTDLISERKVYLLKGKPEKYDPPFRSHLFLTICKVVDTNELL
KSEQLPASERNLDPRLDPRKAKLNNLDAFGIMDYLCKVFTEDKVNDDHDTNRLII
VYMGKRPGRGENASYLAYDKDRTYEEERVYSLRYTGTIPDPNPKD"

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Unknown.  
Unknown.  
Unclassified.  
1 (bases 1 to 1401)  
Hagenson, M. J. and Stromman, D. W.  
Yeast product of streptokinase  
Patent: EP 0241227-1 A1 5.09-DEC-1987;  
Location/Qualifiers  
1..1401  
/organism="unknown"  
/mol\_type="unassigned DNA"

Alignment Scores:  
red. No.: 18.1 Length: 1401  
core: 28.50 Matches: 12  
est. Local Similarity: 34.62% Conservative: 6  
query Match: 23.08% Mismatches: 19  
B: 4.75% Indels: 15  
Gaps: 2

Y - 5 MetValGlnProGlnSerProVal-----AlaValSerGlnSerLysProGlyCysTyr 22  
b 590 ATGGTGTGACCGTAGCTGTAGCTTCAATAGCTTAGTATCTTGAACCTGGTCTGAAA 531

Y - 23 AspAsnGlyLysHistYrClnIleAsnGlnLysTrpGluArgThrLeuGlyAsnVal 42  
b 530 TGGTCATCAGGGTTAAAGGGATAAC----- 504

Y - 43 LeuValCysThrCysThrCysArgGlySerArgGlyPhe 54  
b 503 -----TGTACAGTATATCCACATCAACAGATTC 474

RESULT 20  
STRSKC 2568 bp DNA linear BCT 26-APR-1993  
OCUS Streptococcus equisimilis (H46A) streptokinase gene, complete cds.  
DEFINITION  
K02886.1 GI:153808  
VERSION  
K02886.1  
KEYWORDS  
streptokinase.  
SOURCE Streptococcus dysgalactiae subsp. equisimilis  
Streptococcus dysgalactiae subsp. equisimilis  
Bacteria; Firmicutes; Lactobacillales; Streptococcaceae;  
Streptococcus.  
1 (bases 1 to 2568)  
Malke, H., Roe, B. and Ferretti, J.J.  
Nucleotide sequence of the streptokinase gene from Streptococcus  
equisimilis H46A.  
Gene 34 (2-3), 357-362 (1985)

REFERENCE  
AUTHORS  
TITLE  
JOURNAL  
PUBMED  
COMMENT  
ORGANISM  
DEFINITION  
VERSION  
KEYWORDS  
SOURCE  
STREPTOCOCCUS/C  
OCUS  
DEFINITION  
K02886.1  
VERSION  
K02886.1  
KEYWORDS  
streptokinase.  
SOURCE  
Streptococcus dysgalactiae subsp. equisimilis  
Bacteria; Firmicutes; Lactobacillales; Streptococcaceae;  
Streptococcus.  
1 (bases 1 to 2568)  
Malke, H., Roe, B. and Ferretti, J.J.  
Nucleotide sequence of the streptokinase gene from Streptococcus  
equisimilis H46A.  
Gene 34 (2-3), 357-362 (1985)

ORIGINAL SOURCE text: S. equisimilis (strain H46A) DNA, clone pMP5.  
Draft entry and hard copy of sequence for [1] kindly provided by  
J.J. Ferretti, 03-SEP-1985.  
The -15 and -10 regions are located at positions 760-765 and  
781-786 respectively and an SD sequence at 808-813. Downstream  
from the coding region inverted repeats (positions 2176-2190 and  
2203-2217) are thought to function as transcription terminators.  
The nucleotide sequence of skc does not support the hypothesis that  
the gene has evolved by duplication and fusion, as suggested by  
internal two-fold AA homologies of its product.

Location/Qualifiers  
1..2568  
/organism="Streptococcus dysgalactiae subsp. equisimilis"  
/mol\_type="genomic DNA"  
/db\_xref="taxon:119602"  
794..>2141  
/product="skc mRNA"  
819..2141  
/note="prestreptokinase"  
/codon\_start-1  
/transcriptable1

Unknown.  
Unknown.  
Unclassified.  
1 (bases 1 to 1401)  
Hagenson, M. J. and Stromman, D. W.  
Yeast product of streptokinase  
Patent: EP 0241227-1 A1 5.09-DEC-1987;  
Location/Qualifiers  
1..1401  
/organism="unknown"  
/mol\_type="unassigned DNA"

Alignment Scores:  
red. No.: 18.1 Length: 1401  
core: 28.50 Matches: 12  
est. Local Similarity: 34.62% Conservative: 6  
query Match: 23.08% Mismatches: 19  
B: 4.75% Indels: 15  
Gaps: 2

US-09-940-235-4 (1-259) x STRSKC (1-2568)

Qy 5 MetValGlnProGlnSerProVal-----AlaValSerGlnSerLysProGlyCysTyr 22  
Db 1477 ATGATGTCACCGATGCTAGTGTCTAAATAGCTTAGTATCTTGAACCTGGTCTGAAA 1418

Qy 23 AspAsnGlyLysHistYrClnIleAsnGlnLysTrpGluArgThrLeuGlyAsnVal 42  
Db 1417 TCGTCATCAGGGTTAAAGGGATAAC----- 1391

Qy 43 LeuValCysThrCysThrCysArgGlySerArgGlyPhe 54  
Db 1390 -----TGTACAGTATATCCACATCAACAGATTC 1361

Search completed: December 6, 2004, 15:00:58  
Job time : 5 secs



FT	Region	244..352	PA	(NASC-) NAT SCI COUNCIL.
FT		/note= "Claim 2, see C1"	PI	Wu H;
XX			XX	
PN	WO9407992-A1.		DR	WPI; 1999-189643/16.
XX			DR	N-PSDB; AAX16632.
PD	14-APR-1994.		XX	
XX	05-OCT-1993;	93WO-US009502.	PT	Mutant streptokinase polypeptide - useful as plasmin-resistant thrombolytic agent.
PF			XX	
XX	05-OCT-1992;	92US-00956892.	PS	Claim 1; Col 7-10; 17bp; English.
PR	29-SEP-1993;	93US-00128299.	XX	
XX	(GEHO ) GEN HOSPITAL CORP.		CC	The present invention describes a mutant streptokinase (SK) polypeptide in which at least one of the amino acids in the Pro58-Lys59-Ser60-Dys61 segment of the corresponding native SK is replaced by another amino acid.
PA	(HARD ) HARVARD COLLEGE.		CC	The present sequence represents native SK. SK is a secretory protein of haemolytic Streptococcus able to activate human plasminogen (fibrin) to plasmin (fibrinolysis), which is a serine protease able to catalyse the hydrolysis of fibrin in blood clots. The SK is useful as a thrombolytic agent in the treatment of vascular thromboembolic symptoms such as acute myocardial infarction. Compared with wild-type SK, the K59E mutant is more resistant to degradation by human plasmin and is more effective both in acting as a fibrinolytic agent and in activating human plasminogen. (Updated on 17-OCT-2003 to standardise OS field)
PS			XX	
XX	Reed GL;		CC	Sequence 414 AA;
XX	DR; 1994-135561/16.		CC	Query Match 5.6%; Score 33.5; DB 3; Length 414;
XX	DNA encoding a polypeptide which binds to plasminogen and corresponds to region of streptokinase - useful to detect plasminogen in a sample and to treat myocardial infarction.		CC	Best Local Similarity 29.4%; Pred. No. 0;
PT			CC	Matches 10; Conservative 3; Mismatches 8; Indels 13; Gaps 2;
PT			CC	Query 44 VCTCYGGSRGFNCESKPEAETCF-----DKYT 71
XX			DB	Db 364 IITVYMGKR-----PEGENASYHLLAYDKRYT 390
PS	Disclosure; Page 40-41; 62pp; English.		XX	RESULT 4
XX			ID	AAV01556 standard; peptide; 414 AA.
XX	Nucleic acid comprising a sequence encoding amino acids 14-414 of streptokinase, which binds to plasminogen and does not have a sequence comprising amino acids 60-414 is new. The polypeptide pref. comprises amino acids 244-352, 1-352, 120-352 or 244-414. (Updated on 25-MAR-2003 to correct PN field.) (Updated on 16-OCT-2003 to standardise OS field)		XX	AAV01556;
SQ	Sequence 414 AA;		XX	AAV01556;
XX			XX	
Query	44 VCTCYGGSRGFNCESKPEAETCF-----DKYT 71		XX	
DB	364 IITVYMGKR-----PEGENASYHLLAYDKRYT 390		XX	
XX	RESULT 3		XX	
AAW94664	AAW94664 standard; protein; 414 AA.		XX	
ID			XX	
XX	AAW94664		XX	W0908698-A1.
AC			XX	
XX	AAW94664;		XX	
DT	17-OCT-2003 (revised)		PD	25-FEB-1999.
DT	04-MAY-1999 (first entry)		XX	
XX	Streptococcus equisimilis native streptokinase.		XX	
DE			XX	
XX	Streptococcus equisimilis H46A; streptokinase; mutant; fibrinolytic; plasma clot; hydrolysis; haemolytic Streptococcus; plasminogen; plasmin; vascular protease; fibrin; blood clot; thrombolytic; fibrinolysis; thromboembolic symptom; acute myocardial infarction; fibrinolysis; resistance.		XX	
XX			XX	
OS	Streptococcus dysgalactiae subsp. equisimilis.		XX	
XX			XX	
FH	Key Location/Qualifiers		XX	
FT	Misc-difference 14		XX	
FT	/note= "Encoded by ACC"		XX	
XX	US5876999-A.		XX	
PN	02-MAR-1999.		XX	
XX	PD 06-DEC-1995;	95US-00568393.	PT	New polypeptides which bind streptokinase-specific antibodies - useful in thrombolytic therapy.
XX	PR 06-DEC-1995;	95US-00568393.	XX	Disclosure; Page 12; 44pp; English.
XX		PS		

CC The present sequence represents a native streptokinase. The specification  
 CC describes a polypeptide which binds to a streptokinase-specific antibody  
 CC and prevents the antibody binding to native streptokinase. The  
 CC specification also describes a synthetic polypeptide (P1) comprising an  
 CC epitope which binds to an streptokinase-specific antibody and reduces  
 CC thrombolytic activity of streptokinase. P1 is used in thrombolytic  
 CC therapy, and to prevent or treat Glomerulonephritis and rheumatic fever.  
 CC (Updated on 17-OCT-2003 to standardise OS field)

XX Sequence 414 AA;  
 Query Match 5.6%; Score 33.5; DB 4; Length 414;  
 Best Local Similarity 29.4%; Pred. No. 0;  
 Matches 10; Conservative 3; Mismatches 8; Indels 13; Gaps 2;  
 Qy 44 VCTCYGGSGRNCESKPEAAETCF----DKYT 71  
 Db 364 IITVYMGKR-----PEGENASVHLAYDKDRYT 390

RESULT 5  
 AAY24794 ID AAY24794 standard; protein; 414 AA.  
 AC AAY24794;  
 XX DT 17-OCT-2003 (revised)  
 XX DT 26-AUG-1999 (first entry)  
 DE Streptococcus equisimilis native streptokinase.  
 XX Streptococcus; streptokinase; fibrin-dependent plasminogen activator;  
 KW nsk; rsk; bacterial; blood clot; thrombotic condition;  
 KW myocardial infarction; venous thrombosis; pulmonary embolism;  
 KW cerebral thrombosis; graft thrombosis; arterial thrombosis.  
 OS WO9931247-A1.  
 PN XX 24-JUN-1999.  
 PD XX 15-DEC-1998; 98WO-US026694.  
 PR XX 15-DEC-1997; 97US-0069497P.  
 PA (HARD ) HARVARD COLLEGE.  
 REED GL;  
 PI XX WPI: 1999-395183/33.  
 DR N-PSDB; AAX80492.  
 PT XX N-terminally deleted streptokinase.  
 PS XX Claim 30; Page 60-61; 73pp; English.

CC The present invention describes an isolated bacterial protein that  
 CC induces fibrin-dependent plasminogen activation in a pharmaceutical  
 CC composition for dissolving blood clots. Also described are: (1) a  
 CC composition comprising an isolated modified streptokinase, the  
 CC modification being removal of amino acid residues in the amino terminus;  
 CC (2) a method for dissolving a blood clot in a subject, comprising  
 CC administering to the subject a fibrin-dependent streptokinase protein; a  
 CC nucleic acid (1) encoding a modified bacterial streptokinase; (3) an  
 CC expression vector comprising (1); and (4) a host cell transformed with  
 CC the expression vector of (3). The pharmaceutical composition comprising a  
 CC bacterial fibrin-dependent plasminogen activator is useful for dissolving  
 CC blood clots in patients with a thrombotic condition, e.g. myocardial  
 CC infarction, venous thrombosis, pulmonary embolism, cerebral thrombosis,  
 CC graft thrombosis and arterial thrombosis. The modified streptokinase can  
 CC also be used in non-human mammals. Streptokinase activation of  
 CC plasminogen is at least 10-fold, preferably 100-fold greater in the

CC presence of fibrin than in the absence of fibrin. The modified  
 CC streptokinase has at least one amino acid substitution that inactivates a  
 CC substrate site for proteolytic cleavage. This reduces the rate of  
 CC degradation of the streptokinase at least two-fold. The present sequence  
 CC represents native streptokinase (nSK). (Updated on 17-OCT-2003 to  
 CC standardise OS field)

XX Sequence 414 AA;

Query Match 5.6%; Score 33.5; DB 5; Length 414;

Best Local Similarity 29.4%; Pred. No. 0;  
 Matches 10; Conservative 3; Mismatches 8; Indels 13; Gaps 2;

Qy 44 VCTCYGGSGRNCESKPEAAETCF----DKYT 71

Db 364 IITVYMGKR-----PEGENASVHLAYDKDRYT 390

RESULT 6  
 pct-us93-09502-1

Query Match 5.6%; Score 33.5; DB 7; Length 414;

Best Local Similarity 29.4%; Pred. No. 0;  
 Matches 10; Conservative 3; Mismatches 8; Indels 13; Gaps 2;

Qy 44 VCTCYGGSGRNCESKPEAAETCF----DKYT 71

Db 364 IITVYMGKR-----PEGENASVHLAYDKDRYT 390

RESULT 7  
 us-08-128-299-1

Query Match 5.6%; Score 33.5; DB 8; Length 414;

Best Local Similarity 29.4%; Pred. No. 0;  
 Matches 10; Conservative 3; Mismatches 8; Indels 13; Gaps 2;

Qy 44 VCTCYGGSGRNCESKPEAAETCF----DKYT 71

Db 364 IITVYMGKR-----PEGENASVHLAYDKDRYT 390

RESULT 8  
 us-09-211-542a-6

Query Match 5.6%; Score 33.5; DB 10; Length 414;

Best Local Similarity 29.4%; Pred. No. 0;  
 Matches 10; Conservative 3; Mismatches 8; Indels 13; Gaps 2;

Qy 44 VCTCYGGSGRNCESKPEAAETCF----DKYT 71

Db 364 IITVYMGKR-----PEGENASVHLAYDKDRYT 390

RESULT 9  
 STRP\_STREQ STANDARD; PRT; 440 AA.

XX ID \_STRP\_STREQ AC P00779;  
 XX DT 21-JUL-1986 (Rel. 01, Created)

XX DT 01-APR-1988 (Rel. 07, Last sequence update)

XX DT 01-OCT-2004 (Rel. 45, Last annotation update)

DB Streptokinase C precursor.

GN Name=SKC; OS Streptococcus equisimilis.

OC Bacteria; Firmicutes; Lactobacillales; Streptococcaceae;

OC Streptococcus; [1] NCBI\_TaxID:119602;

RN SEQUENCE FROM N.A.

RP STRAIN=H46A;

RC MEDLINE=232082; PubMed=2989113;

RX MALE H. Roe B.; Ferritti J.J.

RA "Nucleotide sequence of the streptokinase gene from Streptococcus

RT

RT equimimilis H46A";  
 RN Gene 34:357-362 (1985).  
 [2]

SEQUENCE OF 27-440;  
 MEDLINE=83127125; PubMed=6760891;  
 RX Jackson K.W.; Tang J.;  
 RA "Complete amino acid sequence of streptokinase and its homology with  
 RT serine proteases.";  
 RT Biochemistry 21:6120-6625(1982).  
 -!- FUNCTION: This protein is not a protease, but it activates  
 CC plasminogen by complexing with it. As a potential virulence  
 factor, it is thought to prevent the formation of effective fibrin  
 CC barriers around the site of infection, thereby contributing to the  
 CC invasiveness of the cells.

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 CC between the Swiss Institute of Bioinformatics and the BMBL outstation -  
 CC use by non-profit institutions as long as its content is in no way  
 CC modified and this statement is not removed. Usage by and for commercial  
 CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>  
 CC or send an email to license@isb-sib.ch).

CC EMBL; K02986; AAA26974.1; -.  
 DR EMBL; X72832; CAA51351.1; -.  
 DR PIR; A00967; B250.  
 DR PIR; A22801; A22801.  
 DR PDB; 1L4D; X-ray; B=40-173.  
 DR PDB; 1L4Z; X-ray; B=46-173.  
 DR PDB; 1QQR; X-ray; A/B/C/D=177-314.  
 DR InterPro; IPR004093; Staphylokinase.  
 DR InterPro; IPR005124; Streptokinase.  
 DR Pfam; PF02621; Staphylokinase; 3.  
 DR PRINTS; PRO1753; STREPKINASE.  
 DR 3D-structure; Direct protein sequencing; Plasminogen activation;  
 KW Signal; Virulence.  
 FT SIGNAL 1 26  
 FT CHAIN 27 440 Streptokinase C.  
 FT VARIANT 195 195 L -> D.  
 FT VARIANT 207 207 D -> L.  
 FT CONFLICT 300 300 EKX -> LEYK (in Ref. 2).  
 FT CONFLICT 438 438 N -> D (in Ref. 2).  
 FT STRAND 180 180  
 FT STRAND 184 194  
 FT TURN 199 200  
 FT TURN 203 204  
 FT STRAND 205 205  
 FT TURN 209 214  
 FT STRAND 216 217  
 FT STRAND 219 221  
 FT HELIX 222 236  
 FT TURN 238 239  
 FT STRAND 240 252  
 FT TURN 253 254  
 FT STRAND 259 260  
 FT STRAND 268 270  
 FT STRAND 275 275  
 FT STRAND 278 280  
 FT STRAND 282 284  
 FT STRAND 287 289  
 FT STRAND 292 304  
 FT TURN 305 306  
 SQ SEQUENCE 440 AA; 50140 MW; 8FC1F22648ACC77A CRG64;

Query Match 5.6%; Score 33.5; DB 9; Length 440;  
 Best Local Similarity 29.4%; Pred. No. 0;  
 Matches 10; Conservative 3; Mismatches 8; Indels 13; Gaps 2;

Qy 44 VCTCYGGSGFNCESKPEAEETCF-----DKYT 71  
 Db 390 IITVYMGKR-----DGEENASYHLAYDKDRT 416

RESULT 10  
 us-08-560-098a-52

Query Match 5.6%; Score 33.5; DB 11; Length 440;  
 Best Local Similarity 29.4%; Pred. No. 0;  
 Matches 10; Conservative 3; Mismatches 8; Indels 13; Gaps 2;

Qy 44 VCTCYGGSGFNCESKPEAEETCF-----DKYT 71  
 Db 390 IITVYMGKR-----DGEENASYHLAYDKDRT 416

RESULT 11  
 AAY24797 standard; protein; 795 AA.

ID AAY24797  
 AC AAY24797;  
 XX 26-AUG-1999 (first entry)

XX Streptokinase and maltose binding protein fusion protein.

KW Streptococcus; streptokinase; fibrin-dependent plasminogen activator;  
 KW nsk; rsk; bacterial; blood clot; thrombotic condition;  
 KW myocardial infarction; venous thrombosis; pulmonary embolism;  
 KW cerebral thrombosis; graft thrombosis; arterial thrombosis.

XX DE Streptokinase.

XX OS Streptococcus dysgalactiae subsp. equisimilis.

XX OS Synthetic.

XX WO9931247-A1.

XX PN 24-JUN-1999.

XX PD 24-JUN-1999.

XX PR 15-DEC-1998; 98WO-US026624.

XX PR 15-DEC-1997; 97US-0069497P.

XX PA (HARD ) HARVARD COLLEGE.

XX PA Reed GL;

XX PR WPI; 1999-395183/33.

XX DR N-PSDB; AAX80497.

XX PT N-terminally deleted streptokinase.

XX PS Example; Page 48-51; 73pp; English.

XX The present invention describes an isolated bacterial protein that  
 CC induces fibrin-dependent plasminogen activation in a pharmaceutical  
 CC composition for dissolving blood clots. Also described are: (1) a  
 CC composition comprising an isolated modified streptokinase, the amino terminus;  
 CC modification being removal of amino acid residues in the amino terminus;  
 CC (2) a method for dissolving a blood clot in a subject comprising  
 CC administering to the subject a fibrin-dependent streptokinase protein; a  
 CC nucleic acid (1) encoding a modified bacterial streptokinase; (3) an  
 CC expression vector comprising (1); and (4) a host cell transformed with  
 CC the expression vector of (3). The pharmaceutical composition comprising a  
 CC bacterial fibrin-dependent plasminogen activator is useful for dissolving  
 CC blood clots in patients with a thrombotic condition, e.g. myocardial  
 CC infarction, venous thrombosis, pulmonary embolism, cerebral thrombosis,  
 CC graft thrombosis and arterial thrombosis. The modified streptokinase can  
 CC also be used in non-human mammals. Streptokinase activation of  
 CC plasminogen is at least 10-fold greater in the  
 CC presence of fibrin than in the absence of fibrin. The modified  
 CC streptokinase has at least one amino acid substitution that inactivates a  
 CC substrate site for proteolytic cleavage. This reduces the rate of  
 CC degradation of the streptokinase at least two-fold. The present sequence  
 CC represents a streptokinase and maltose binding protein fusion protein  
 XX from an example of the present invention

SQ Sequence 795 AA;

Query Match Similarity 5.6%; Score 33.5; DB 6; Length 795;  
Best Local Similarity 29.4%; Pred. No. 0;  
Matches 10; Conservative 3; Mismatches 8; Indels 13; Gaps 2;  
Matches 10; Conservative 3; Mismatches 8; Indels 13; Gaps 2;

Qy 44 VCTCYGGSRGFNCBSKPKAABETCP-----DKYT 71  
Db 745 IITVYMGKR-----PEGENASYHLAYDKDRYT 771

RESULT 12  
us-09-211-542a-2

Query Match Similarity 5.6%; Score 33.5; DB 12; Length 795;  
Best Local Similarity 29.4%; Pred. No. 0;  
Matches 10; Conservative 3; Mismatches 8; Indels 13; Gaps 2;  
Matches 10; Conservative 3; Mismatches 8; Indels 13; Gaps 2;

Qy 44 VCTCYGGSRGFNCBSKPKAABETCP-----DKYT 71  
Db 745 IITVYMGKR-----PEGENASYHLAYDKDRYT 771

Search completed: December 6, 2004, 14:53:45  
Job time : 1 secs

Copyright (c) 1993 - 2004 Compugen Ltd.	GenCore version 5.1.6	Streptokinase and Streptococcus equi					
OM protein - nucleic search, using frame_plus_p2n model	December 6, 2004, 15:02:16 ; Search time 2 Seconds (without alignments)	ACCESSION: E03308 ACCESSION: I05204 ACCESSION: K02886 ACCESSION: E03308					
Run on:	US-09-940-235-4	2.629 Million cell updates/sec					
Title:	US-09-940-235-4						
Perfect score:	627						
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Ygapop	0.0	Ygapext	0.5				
Fgapop	6.0	Fgapext	7.0				
Delop	6.0	Delext	7.0				
Searched:	10 seqs, 23900 residues						
Total number of hits satisfying chosen parameters:	20						
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Maximum DB seq length:	2000000000						
Post-processing:	Minimum Match 0%						
Maximum Match 100%							
Listing first 20 summaries							
Command line parameters:							
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	2: /staff_overflow/sdavid-tmp/deco0/swope235/seq/03308_gb.pat:*						
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c 1	41	6.5	8931	4	SEDEXB		ACCESSION: X72832
c 2	39	6.2	8931	4	SEDEXB		Streptococcus equi
c 3	33.5	5.3	1242	6	AAJ16632		Streptococcus equi
c 4	33.5	5.3	1242	7	AAY80492		Streptococcus equi
c 5	33.5	5.3	1242	9	us-09-211-542a-5		Streptokinase and Streptococci
c 6	33.5	5.3	1242	10	us-08-568-393b-1		Streptokinase and Streptococci
c 7	33.5	5.3	1401	3	I05204		ACCESSION: I05204
c 8	33.5	5.3	2385	1	AR43998		ACCESSION: AR43998
c 9	33.5	5.3	2385	8	AAJ80497		ACCESSION: AR43998
c 10	33.5	5.3	2568	5	2385		ACCESSION: AR43998
c 11	33.5	5.3	2568	1	AAJ80497		ACCESSION: AR43998
ALIGMENTS							
RESULT 1							
SEDEXB/c							
LOCUS	S equi similis dexb, abc, lrp, skc, rel genes and ORFL.						
DEFINITION							
ACCESSION	X72832_1						
VERSION	GI:407876						
KEYWORDS	abc gene; ABC transporter; dexb gene; dextran glucosidase; glucan 1,6-alpha-glucosidase; lecine rich protein; lrp gene; ORFL; rel gene; skc gene; streptokinase; stringent response-like protein.						
SOURCE							
ORGANISM	Streptococcus dysgalactiae subsp. equisimilis						
STREPTOCOCCUS	Bacteria; Firmicutes; Lactobacillales; Streptococcaceae;						
REFERENCE	1 (bases 3621 to 6190)						
AUTHORS	Malke, H., Roe, B. and Ferretti, J.J.						
TITLE	Nucleotide sequence of the streptokinase gene from Streptococcus equisimilis H46A						
JOURNAL	Gene 34 (2-3), 357-362 (1985)						
MEDLINE	85232082						
PUBMED	2989113						
REFERENCE	2 (bases 1 to 4188; 5790 to 8931)						
AUTHORS	Mechoild, U., Steiner, K., Vettermann, S. and Malke, H.						
TITLE	Genetic organization of the streptokinase region of the Streptococcus equisimilis H46A chromosome						
JOURNAL	Mol. Gen. Genet. 241 (1-2), 129-140 (1993)						
MBID	94049672						
PUBMED	8232196						
REFERENCE	3 (bases 1 to 8931)						
AUTHORS	Malke, H.						
TITLE	Direct Submission						
JOURNAL	Submitted (05-MAY-1993) H. Malke, Institute for Molecular Biology, Jena University, Winterlaer Str 10, 07078 Jena, FRG						
COMMENT	Related sequences: M19346, X13399 & X13400.						
FEATURES	Location/Qualifiers						
Source							
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terminator							
CDS							
SUMMARIES							
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RBS	
terminator	
misc_feature	
CDS	
misc_feature	
RBS	
terminator	





agent in the treatment of vascular thromboembolic symptoms such as acute myocardial infarction. Compared with wild type SK, the K59S mutant is more resistant to degradation by human plasmin and is more effective both in acting as a fibrolytic agent and in activating human plasminogen.

(Updated on 17-Oct-2003 to Standardise OS field)

Sequence 1242 BP; 423 A; 268 C; 237 G; 314 T; 0 U; 0 Other;

Alignment Scores:

Pred. No.: 2.19 Length: 1242  
Score: 33.50 Matches: 10  
Percent Similarity: 41.94% Conservative: 3  
Best Local Similarity: 32.26% Mismatches: 6  
Query Match: 5.34% Indels: 12  
DB: 6 Gaps: 1

US-09-940-235-4 (1-259) x AAX16632 (1-1242)

Qy 168 GluThrTrpGlu-LysProTyrglnGlyTrpMetMetValAspCysThr----- 183  
ID 537 GAGACCTGTCGAAATGGTCATGGGTTAACGGAGTAACCTACAGTATATTCCAC 478

Qy 184 -----CysLeuGly 186

Db 477 ATCAACAGATTTCGCTGGTTTGATTCGT 447

RESULT 4

AAX80492/c  
ID AAX80492 standard; cDNA; 1242 BP.  
XX

AC AAX80492;

XX DT 17-OCT-2003 (revised)

DT 26-AUG-1999 (first entry)

DE Streptococcus equisimilis native streptokinase encoding cDNA.

XX Streptococcus; streptokinase; fibrin-dependent Plasminogen activator;  
KW rSK; bacterial; blood clot; thrombotic condition;  
KW myocardial infarction; venous thrombosis; pulmonary embolism;  
KW cerebral thrombosis; graft thrombosis; arterial thrombosis; 88.  
XX Streptococcus dysgalactiae subsp. equisimilis.  
OS W09931247-A1.

PN 24-JUN-1999.

XX 15-DEC-1998; 98WO-US0266594.

XX 15-DEC-1997; 97US-0069497P.

XX (HARD ) HARVARD COLLEGE.

XX Reed GL;

PI DR; 199-395183/33.

XX P-PSDB; AA24794.

XX N-terminally deleted streptokinase.

XX Claim 44; Page 58-60; 73pp; English.

XX The present invention describes an isolated bacterial protein that

XX induces fibrin-dependent plasminogen activation in a pharmaceutical

XX composition for dissolving blood clots. Also described are: (1) a

XX modification comprising an isolated modified streptokinase, the

XX modification being removal of amino acid residues in the amino terminus;

XX (2) a method for dissolving a blood clot in a subject, comprising

XX administering to the subject a fibrin-dependent streptokinase protein;

XX (3) an nucleic acid (1) encoding a modified bacterial streptokinase;

XX (4) a host cell transformed with

XX the expression vector of (3). The pharmaceutical composition comprising a

CC bacterial fibrin-dependent plasminogen activator is useful for dissolving  
CC blood clots in patients with a thrombotic condition, e.g. myocardial  
CC infarction, venous thrombosis, pulmonary embolism, cerebral thrombosis,  
CC graft thrombosis and arterial thrombosis. The modified streptokinase can  
CC also be used in non-human mammals. Streptokinase activation of  
CC plasminogen is at least 10-fold, preferably 100-fold greater in the  
CC presence of fibrin than in the absence of fibrin. The modified  
CC streptokinase has at least one amino acid substitution that inactivates a  
CC substrate site for proteolytic cleavage. This reduces the rate of  
CC degradation of the streptokinase at least two-fold. The present sequence  
CC encodes native streptokinase (nSK). (Updated on 17-OCT-2003 to  
CC standardise OS field)

SQ Sequence 1242 BP; 424 A; 267 C; 314 G; 314 T; 0 U; 0 Other;

Alignment Scores:

Pred. No.: 2.19 Length: 1242  
Score: 33.50 Matches: 10  
Percent Similarity: 41.94% Conservative: 3  
Best Local Similarity: 32.26% Mismatches: 6  
Query Match: 5.34% Indels: 12  
DB: 7 Gaps: 1

US-09-940-235-4 (1-259) x AAX80492 (1-1242)

Qy 168 GluThrTrpGlu-LysProTyrglnGlyTrpMetMetValAspCysThr----- 183

ID 537 GAGACCTGTCGAAATGGTCATGGGTTAACGGAGTAACCTACAGTATATTCCAC 478

Qy 184 -----CysLeuGly 186

Db 477 ATCAACAGATTTCGCTGGTTTGATTCGT 447

RESULT 5  
us-09-211-542a-5/c

Alignment Scores:

Pred. No.: 2.19 Length: 1242  
Score: 33.50 Matches: 10  
Percent Similarity: 41.94% Conservative: 3  
Best Local Similarity: 32.26% Mismatches: 6  
Query Match: 5.34% Indels: 12  
DB: 9 Gaps: 1

US-09-940-235-4 (1-259) x AAX80492 (1-1242)

Qy 168 GluThrTrpGlu-LysProTyrglnGlyTrpMetMetValAspCysThr----- 183

ID 537 GAGACCTGTCGAAATGGTCATGGGTTAACGGAGTAACCTACAGTATATTCCAC 478

Qy 184 -----CysLeuGly 186

Db 477 ATCAACAGATTTCGCTGGTTTGATTCGT 447

RESULT 6  
us-08-568-393b-1/c

Alignment Scores:

Pred. No.: 2.19 Length: 1242  
Score: 33.50 Matches: 10  
Percent Similarity: 41.94% Conservative: 3  
Best Local Similarity: 32.26% Mismatches: 6  
Query Match: 5.34% Indels: 12  
DB: 10 Gaps: 1

US-09-940-235-4 (1-259) x us-08-568-393b-1 (1-1242)

Qy 168 GluThrTrpGlu-LysProTyrglnGlyTrpMetMetValAspCysThr----- 183

ID 537 GAGACCTGTCGAAATGGTCATGGGTTAACGGAGTAACCTACAGTATATTCCAC 478

Qy 184 -----CysLeuGly 186

Db 477 ATCAACAGATTTCGCTGGTTTGATTCGT 447

Db	477	ATCAACAGATTTCGCTTGGTTTGTATTGGT	447
RESULT	7		
105204/c			
LOCUS	105204	Sequence 5 from Patent EP 0248227.	
DEFINITION		1401 bp	DNA
ACCESSION	105204	EP 0248227.	
VERSION	105204.1	GI:591209	
KEYWORDS	.		
SOURCE	Unknown.		
ORGANISM	Unknown.		
UNCLASSIFIED			
REFERENCE	1	(bases 1 to 1401)	
AUTHORS	Hagenson, M.J. and Stroman, D.W.		
TITLE	Yeast Production of streptokinase		
JOURNAL	Patent : EP 0248227-A1 5 09-DEC-1987;		
FEATURES	Location,Qualifiers		
source	1..1401		
		/organism="unknown"	
		/mol type="unassigned DNA"	

RESULT 8	AR143998/c	AR143998	Sequence 1	from patent	2385 bp	DNA	linear
DEFINITION							
ACCESSION	AR143998						
VERSION	AR143998.1						
KEYWORDS							
SOURCE	Unknown.	Unclassified.					
ORGANISM	Unknown.	Unclassified.					
REFERENCE	1 (bases 1 to 2385)						
AUTHORS	Reed,G.L.						
TITLE	Bacterial fibrin-dependent plasminogen activator						
JOURNAL	Patent: US 6210667 A 1 03-APR-2001;						
FEATURES	Location/Qualifiers						
source	1. 2385						
	/organism="unknown"						

Bilancio Comunale

DB:	1	DB:	1
Pred. No.:	10	Length:	2385
Score:	33.50	Matches:	10
Percent Similarity:	41.94%	Conservative:	3
Best Local Similarity:	32.26%	Mismatches:	6
Query Match:	5.34%	Indels:	12
		Gaps:	1
US-09-940-235-4 (1-259) x AR143998 (1-2185)			
Qy	168 GluThrPrglu-LysProTyrglnGlyTrpMetMetvalAspCysThr-----		183
Db	1680 GAGACCTGGCTGAAATCGTCAATCGGTAACTGACAGTATATTCCAC		1621
Qy	184 -----CysteauGly		186

Db	1620	ATCACAGATTTCGGTTGGTTGGATTGGT	1590
	RESULT 9		
	AAX80497/C		
	ID AAX80497	standard; cDNA; 2385 BP.	
	XX		
	AC		
	AAX80497;		
	XX		
	DT	(first entry)	
	XX		
	DE	Streptokinase and maltose binding protein fusion	
	XX		
	KW	Streptococcus; streptokinase; fibrin-dependent	
	KW	NSK; rSK; bacterium; blood clot; thrombotic co-	
	KW	myocardial infarction; venous thrombosis; pulmonary	
	KW	cerebral thrombosis; graft thrombosis; arterial	
	XX		
	OS	Streptococcus dysgalactiae subsp. equisimilis	
	OS	synthetic.	

PN	WO931247-A1.
XX	
PD	24-JUN-1999.
XX	
PF	15-DEC-1998;
XX	98WO-US026694.
PR	15-DEC-1997;
XX	97US-0069497P.
PA	(HARD ) HARVARD COLLEGE.
XX	
PI	Reed GL;
XX	
WPI	1999-3951-83 /33 .
DR	
P-PSDB	AAV24197 .
XX	
N-terminally deleted streptokinase.	
XT	

The present invention describes an isolated bacterial protein that induces fibrin-dependent plasminogen activation in a pharmaceutical composition for dissolving blood clots. Also described are: (1) a composition comprising an isolated modified streptokinase, the modification being removal of amino acid residues in the amino terminus; (2) a method for dissolving a blood clot in a subject, comprising protein: a administering to the subject a fibrin-dependent streptokinase protein; a nucleic acid (1) encoding a modified bacterial streptokinase; (3) an expression vector comprising (1); and (4) a host cell transformed with the expression vector of (3). The pharmaceutical composition comprising a bacterial fibrin-dependent plasminogen activator is useful for dissolving blood clots in patients with a thrombotic condition, e.g. myocardial infarction, venous thrombosis, pulmonary embolism, cerebral thrombosis, graft thrombosis and arterial thrombosis. The modified streptokinase can also be used in non-human mammals. Streptokinase activation of plasminogen is at least 10-fold, preferably 100-fold greater in the presence of fibrin. The modified streptokinase is useful in the absence of fibrin.

CC streptokinase has at least one amino acid substitution that inactivates  
 CC substrate site for proteolytic cleavage. This reduces the rate of  
 CC degradation of the streptokinase at least two-fold. The present sequence  
 CC encodes a streptokinase and maltose binding protein fusion protein from  
 CC an example of the present invention

US-09-940-235-4 (1-259) x AAX80497 (1-2385)

Qy 168 GluthrTrpGlu-LysPrtryGlnGlyTrpMetMetValAspCysThr----- 183

Db 1433 GAGCTCTGCTGAAATCGTCATGGGAGTAACCTACAGTATAATTCCAC 1374

Qy 1680 GAGACCTGCTGCTGAAATCGTCATGGGAGTAACCTACAGTATAATTCCAC 1621

Qy 184 -----CysLysLys 186

Db 1620 ATGACAGATTTCGCTTGGTTGATGTT 1590

RESULT 1.0

STRSKC/C LOCUS STRSKC 2568 bp DNA linear BCT 26-APR-1993

DEFINITION Streptococcus equisimilis (H46A) streptokinase gene, complete cds.

ACCESSION K02985

VERSION K02986.1 GI:1533808

KEYWORDS streptokinase

SOURCE Streptococcus dysgalactiae subsp. equisimilis

ORGANISM Streptococcus dysgalactiae subsp. equisimilis

Bacteria; Firmicutes; Lactobacillales; Streptococaceae;

Streptococcus.

(bases 1 to 2568)

Malce, H., Roe, B. and Ferretti, J.J.

Nucleotide sequence of the streptokinase gene from Streptococcus equisimilis H46A

REFERENCE 34 (2-3), 357-362 (1985)

AUTHORS

TITLE

JOURNAL MEDLINE 85233082

PUBMED 2989113

COMMENT Original source text: *S. equisimilis* (strain H46A) DNA, clone pMFS. Draft entry and hard copy of sequence for [1] kindly provided by J.J. Ferretti, 03-SEP-1985.

The -35 and -10 regions are located at positions 760-765 and 781-786 respectively and an SD sequence at 808-813. Downstream from the coding region inverted repeats (positions 2176-2190 and 2203-2217) are thought to function as transcription terminators.

The nucleotide sequence of skc does not support the hypothesis that the gene has evolved by duplication and fusion, as suggested by internal two-fold AA homologies of its product.

FEATURES

source

1..2568 /organism="Streptococcus dysgalactiae subsp. equisimilis"

/mol type="genomic DNA"

/db\_xref="taxon:119602"

/product="cDNA"

mRNA

CDS

819 .. 2141 /note="prestreptokinase"

/codon\_start=1

/trans\_table=11

/protein\_id="AA126974.1"

/db\_xref="GI:153809"

/c\_translation="MKNLISFPMALLFALFTGTUNVQAGPWEILDPPEVNSOL

VVSAGTVEGTMQDISKFFDLTRSPKPFATDSGAMSHKLUK

ADLLKAIQOBULANVHSNDYEVITDASDGTIDTRNGKVKYFPAKDGDSVTLTQPOIE

PLLSGHVTRPKKEKPNQQAMSVDVEYTIQTPPLANDDDFRPLKDTKLKLTAGD

TITSQBEILAQASILRNKHPGTDKQDTRDNTDNDLFRILPMDOEFTRVKNREQ

AYRINKQSKQAGNEBNNLTDISKYKVKKGKPYDPRSHKLFKLKVWDNTNEIL

KSEQLLITASBNLDFRDYDPDKAKLYNNNDIAGIMDYLTKYEDNHDNTNRIIT

VMGKRPGENASYHAYDKDRTYEEREVYSLYRTGTPIDNPNDK"

sig\_peptide 819 .. 896 /note="streptokinase signal peptide"

mat\_peptide 897 .. 2138 /product="streptokinase"

Alignment Scores:

Pred. No.: 11..5 Length: 2568

Score: 33..50 Matches: 10

Percent Similarity: 41..94% Conservative: 3

Best Local Similarity: 32..26% Mismatches: 6

Query Match: 5..34% Indels: 12

DB: 5 Gaps: 1

US-09-940-235-4 (1-259) x STRSKC (1-2568)

Qy 168 GluthrTrpGlu-LysPrtryGlnGlyTrpMetMetValAspCysThr----- 183

Db 1433 GAGCTCTGCTGAAATCGTCATGGGAGTAACCTACAGTATAATTCCAC 1374

Qy 184 -----CysLysLys 186

Db 1373 ATCAACAGATTTCGCTTGGTTGTTGTTGGT 1343

RESULT 1.1

AR143998 LOCUS AR143998 Sequence 1 from patent US 6210667.

DEFINITION AR143998

ACCESSION AR143998

VERSION AR143998.1 GI:15105865

KEYWORDS Unknown.

SOURCE Unknown.

ORGANISM Unclassified.

REFERENCE 1 (bases 1 to 2385)

AUTHORS Red, G. L.

TITLE Bacterial fibrin-dependent plasminogen activator

JOURNAL Patent: US 6210667-A 1-03-APR-2001;

FEATURES Location/Qualifiers 1..2385

Source /organism="unknown"

/mol\_type="unassigned DNA"

Alignment Scores:

Pred. No.: 12..8 Length: 2385

Score: 33..00 Matches: 22

Percent Similarity: 30..98% Conservative: 10

Best Local Similarity: 20..75% Mismatches: 42

Query Match: 5..26% Indels: 32

DB: 1 Gaps: 5

US-09-940-235-4 (1-259) x AR143998 (1-2385)

Qy 151 IleAlaGluLysCysPheAspHisAlaAlaGlyThrSerTyValValGlyGluThrTrp 170

Db 907 GTAGGCTGAGTCTACAGGAGAAGTGGCAAGATCACGTTATGCCGACCATG 966

Qy 171 GluLysPrtryGlnGly-----TrpMet 178

Db 967 GAAAGGCCAACAGGGAAATCTGCCAACATCCGGAGATGTCCTTTGGTAT 1026

Qy 179 MetValAspCysThrCysLysGluGlyLysGlyArgLysLysCysThrSerArgAla 198

Db 1027 GCGGCGCTACTGGGTATCAACGCCGCGCAGCGCTCGTCAGCTGTCGAT-----GAA 1080

Qy 199 ArgCysAsnAspGlnAspThrArgThrSerTyArgLysGlyAspThrTrpSerLysS 218

Db 1081 GCCCTGAAAGACGCCAGACTAAATCGAGTCGGTACCCGC----- 1122

Qy 219 AspAsnArgGlyAsnLeuLeuGlnCysIleCysThrGlyAsnGlyArg-----Gly 235

Db 1123 -----CGGGGATCCATC-----GAGGTAGGATTGCTGACCT 1155

Qy 236 GluTrpLysCysGluArg 241

Db 1156 GAGTGGCTGCTAGACCGT 1173

RESULT 1.2

ARX80497 ID AAX80497 standard; cDNA; 2385 BP.

XX

AC AAX80497;

DT 26-AUG-1999 (first entry)

XX

DB Streptokinase and maltose binding protein fusion protein encoding cDNA.

XX

KW Streptococcus, streptokinase; fibrin-dependent plasminogen activator;





Qy	221 ArgGlyAsnLeuLeu-----GlnCysIleCysThrGlyAsnGlyArgGlyGluTrp 237	Db	609 -----CTCCCTGGCTAGGCAAGTCTATCTGAAACAAACATCCGGGTACACT 659
Db	595 -----TTACTAGTCGCAAGCAAAACATTTAACAAAACCCAGGTATACG 645	Qy	238 LysCysGluArgHisThrSerValGlnThr 247
Qy	238 LysCysGluArgHisThrSerValGlnThr 247	Db	660 ATCTAGCAACGCACTCTCCATGTAACC 689
Db	646 ATTATGAACTGTAATGTCGTCAT 675	RESULT 18	
RESULT 17		105204	105204 Sequence 5 from Patent EP 0248227. 1401 bp DNA linear
E03308	E03308 1262 bp DNA encoding recombinant streptokinase.	DEFINITION	105204 Sequence 5 from Patent EP 0248227. 1401 bp DNA linear
LOCUS	E03308	ACCESSION	105204 Sequence 5 from Patent EP 0248227.
DEFINITION	E03308	VERSION	105204.1 GI:591209
VERSION	E03308.1 GI:2171525	KEYWORDS	Unknown.
KEYWORDS	1 (bases 1 to 1262)	ORGANISM	Unclassified.
ORGANISM	synthetic construct	REFERENCE	1 (bases 1 to 1401)
REFERENCE	JP 1992011892-A/1.	AUTHORS	Hagenson, M.J. and Stroman, D.W.
AUTHORS	Fuji, S., Katano, T., Majima, E., Ogino, K., Ono, K., Sakata, Y. and UenoYama, T.	TITLE	Sequence Production of Streptokinase
TITLE	PROTEIN OF STREPTOKINASES, CORRESPONDING GENE, CORRESPONDING PLASMID RECOMBINANT, CORRESPONDING CHARACTER TRANSFORMANT AND PRODUCTION	FEATURES	Patent: EP 0248227-A1 5-09-DEC-1987;
JOURNAL	Patent: JP 1992011892-A 1 16-JAN-1992;	source	Location/Qualifiers
COMMENT	OS Artificial gene	Alignment Scores:	
OS	Artificial sequence ; Genes .	Pred. No. :	10 5 Length: 1401
OC	JP 1992011892-A/1	Score:	31.50 Matches: 16
PN	16-JAN-1992	Percent Similarity:	48.00 %
PD	06-JUL-1990	Best Local Similarity:	32.00 %
PF	11-APR-1989 JP 90P 96530	Query Match:	5.02 %
PR	11-APR-1989 JP 90P 96530	DB:	3
PI	FUJII, SETSUO, KATANO, TAMIYAKA, MAJIMA, EIJI, OGINO, KOICHI, PI	US-09-940-235-4 (1-259) x 105204 (1-1401)	Length: 1401
ONO, KENJI,	SAKATA, YASUO, UENOYAMA, TSUTOMU	Qy	203 GlnAspThrArg-----ThrSerTyrArgIleGlyAspThrTrpSerLysAspAsn 220
PC	C12N15/58, C12N1/21, C12N9/70, (C12N1/21, C12R1:19), (C12N9/70, PC C12R1:19);	Db	547 AAAGATACATAAGCTATGAAACACTAGTATCGTGAACCATCACATCTCAAGAA--- 603
CC	strandedness: Double;	Qy	221 ArgGlyAsnLeuLeu-----GlnCysIleCysThrGlyAsnGlyArgGlyGluTrp 237
CC	topology: Linear;	Db	604 -----TTACTAGCTCAAGCAAAACCATTAAACAAAACACCAGGTATACG 654
CC	hypothetical: No;	Qy	238 LysCysGluArgHisThrSerValGlnThr 247
CC	anti-sense: No;	Db	655 ATTATGAACTGTAATGTCGTCAT 689
CC	*source: clone-PSKX;	RESULT 19	
FH	key	STRSKC	2568 bp DNA linear
FH	5'UTR	LOCUS	BCT 26-APR-1993
FT	CDS	DEFINITION	Streptococcus equisimilis (H46A) streptokinase gene, complete cds.
FT	12 . 1256	ACCESSION	K02986
FT	/product= recombinant streptokinase' FT	VERSION	K02986.1 GI:153808
FT	1253	KEYWORDS	Streptococcus streptokinase subsp. equisimilis
mat_peptide	12 . 1256	SOURCE	Streptococcus dysgalactiae subsp. equisimilis
FT	/product= recombinant streptokinase' FT	ORGANISM	Bacteria: Firmicutes; Lactobacillales; Streptococcaceae; Streptococcus
FT	1257 . 1263	REFERENCE	1 (bases 1 to 2568)
3'UTR	Location/Qualifiers	AUTHORS	Malke, H., Roe, B. and Ferretti, J.J.
FEATURES	1 . 1262	TITLE	Nucleotide sequence of the streptokinase gene from Streptococcus equisimilis H46A
source	/organism= synthetic construct "	JOURNAL	Gene 34 (2-3) , 357-362 (1985)
	/mol_type= genomic DNA,"	MEDLINE	85232082
	/db_xref="axon.32630"	PUBMED	2989113
		COMMENT	Original source text: <i>S. equisimilis</i> (strain H46A) DNA, clone PMF5. Draft entry and hard copy of sequence for [1] kindly provided by J.D. Ferretti, 03-SEP-1985.
Qy	203 GlnAspThrArg-----ThrSerTyrArgIleGlyAspThrTrpSerLysAspAsn 220		The -35 and -10 regions are located at positions 760-765 and 781-786 respectively and an SD sequence at 808-813. Downstream from the coding region inverted repeats (positions 2176-2190 and 2203-2217) are thought to function as transcription terminators.
Db	552 AAAGACACTAAACTGCTGCAAAACCTGSGTATCGTGAACCATCTCTGAGGAG-- 608		
Qy	221 ArgGlyAsnLeuLeu-----GlnCysIleCysThrGlyAsnGlyArgGlyGluTrp 237		

The nucleotide sequence of *sikc* does not support the hypothesis that the gene has evolved by duplication and fusion, as suggested by internal two-fold AA homologies of its product.

## FEATURES SOURCE

1. 2568 /organism="Streptococcus dysgalactiae subsp. equisimilis"

/mol\_type="genomic DNA"

/db\_xref="taxon:119602"

/product="sikc mRNA"

819 . . 2141

/note="prestreptokinase"

/codon\_start=1

/translate\_table=11

/protein\_id="AAA26974.1"

/db\_xref="GI:153809"

/translation="MKNYLSPOMFALLFALTFGTGVNSVQALAGPENWLLDPSVNNSQL  
VVSAGTVEGINODISIUKFFEDLTISPAHGGTEEQUSPSKSPFATDGSANSHKLUK  
ADLLRATQEQLIANYKNDYFEVIDEVSFASDASDITDNGKDPFDGKDSVTLKLTLLG  
FLISCHGHRVVRPKYKEKQDQNSDQKSKVDEYTVQPTPLAPDPPGKLDKDTKLKLTLLG  
TITSQELLAQASILLNKNHGPGTIVYERDSSITVHDNDI FRTLPLMDDGFTYRVKRNREQ  
AYRINKKLSERNLNEDFNDLQKLYKFLTKYVVDTNEIL  
KSBOLITASERNLNEDFNDLQDPRDKAKLYNNDIAGIMDYLTKYVEDNHDNTNIRIT  
VIMGKRPGEVASYLHAYDKDRTYEEREVSYLRTGTPIDNPNDK"

819 . . 896

/note="streptokinase signal peptide"

897 . . 2138

/product="streptokinase"

Alignment Scores:

Pred. No. : 19 . 6

Length: 2568

Score: 31 . 50

Matches: 16

Percent Similarity: 48 . 00%

Conservative: 8

Best Local Similarity: 32 . 00%

Mismatches: 17

Query Match: 5 . 02%

Indels: 9

DB: 5

Gaps: 3

US-09-940-235-4 (1-259) x E03308 (1-1262)

Qy 221 ArgGlyAsnLeuGlnCysIleCysThr--GlyAsnGlyArgGlyGlu----- 236

Db 188 CGGGACAGGCCCTTCCGTTTACCACTATGCCGACGAGGGTCAGGTGATTTC 129

Qy 237 TrpLysCysGluArgHistidineSerValGlnThrSerGlySer 252

Db 128 GAAAGATTTCAGAGATGTCTCGGTTAGTACCTCAACAGTGCCAGC 81

Search completed: December 6, 2004, 15:02:22

Job time : 6 secs

RESULT 20  
E03308/C LOCUS E03308 1262 bp DNA linear PAT 29-SEP-1997  
DEFINITION DNA encoding recombinant streptokinase.  
ACCESSION E03308  
VERSION E03308.1 GI:2171525  
KEYWORDS JP 1992011892-A/1  
SOURCE Synthetic construct  
ORGANISM Streptococcus suis  
REFERENCE 1 (bases 1 to 1262)  
AUTHORS Fujii,S., Katano,T., Majima,E., Ogino,K., Ono,K., Sakata,Y. and UenoYama,T.  
TITLE PROTEIN OF STREPTOKINASES, CORRESPONDING GENE, CORRESPONDING PLASMID RECOMBINANT, CORRESPONDING CHARACTER TRANSFORMANT AND PRODUCTION  
JOURNAL Patent: JP 1990-011892-A 1 16-JAN-1992;  
COMMENT OS Artificial gene  
OC Artificial sequence; Genes.  
PN JP 1992011892-A/1  
PD 16-JAN-1992



Qy	151	IAEKCFDHAAGTSSYVGVGETKPYQG-----WMMVDCTCLGBGSGRITCTSRN 198	Score 33; DB 12; Length 795;	DT XX	16-NOV-1994 (first entry)
Db	303	VALKSYEEBLAKDPRIAMENAQORGEMIPNIPOMSAFFYAVRTAVINASGRQTVB 360	Best Local Similarity 20.8%; Prod. No. 0.38; Mismatches 42; Indels 32; Gaps 5;	DE XX	Streptokinase.
Qy	199	RNDQDFTTSYRIGDTWNSKDKDNRGNLQQCJCTGNR-----GEWCER 241	WMMVDCTCLGBGSGRITCTSRN 198	XX	Streptokinase; SK; Streptococcus equisimilis; plasminogen; myocardial infarction.
Db	361	ALKDAQTNSSVFG-----RGSI-----EGRIAGPENLDR 391	XX	XX	Streptococcus dysgalactiae subsp. equisimilis.
<b>RESULT 3</b>					
AAR10194			Location/Qualifiers		
ID	AAR10194	standard; protein; 414 AA.	FT Region	1. .352	/note= "claim 3, see CC"
XX			FT Region	14. .414	/note= "claim 1, see CC"
AC			FT Region	120. .352	/note= "claim 1, see CC"
XX			FT Region	244. .414	/note= "claim 3, see CC"
DT	28-MAR-1991	(first entry)	FT Region	244. .352	/note= "claim 2, see CC"
XX			PN	WO9407932-A1.	
DE		Streptokinase encoded by synthetic gene.	XX		
XX		streptokinase; thrombolytic agent; myocardial infarction.	PD	14-APR-1994.	
KW			XX		
XX			PP	05-OCT-1993;	93WO-US009502.
OS			XX	05-OCT-1992;	92US-00956692.
XX			PR	29-SEP-1993;	93US-00128299.
PN	EP407942-A.		XX		
XX			(GEHO ) GEN HOSPITAL CORP.		
PD	16-JAN-1991.		PA		
XX			(HARD ) HARVARD COLLEGE.		
PF	11-JUL-1989;	89JJP-00179432.	XX		
XX			PI	Reed GL;	
PR	11-JUL-1989;	89JJP-00179432.	XX		
PR	27-NOV-1989;	89JJP-00307987.	DR	WPI; 1994-135561/16.	
PR	11-APR-1990;	90JJP-00096830.	XX		
XX			PT	DNA encoding a polypeptide which binds to Plasminogen and corresponds to	
PA	(SAKA ) OTSUKA PHARM FACTOR.		PT	region of streptokinase - useful to detect Plasminogen in a sample and to	
XX			PT	treat myocardial infarction.	
PI	Majima E, Ogino K, Ono K, Sakata Y, Uenoyama T;		PS	Disclosure; Page 40-41; 62pp; English.	
XX			XX		
DR	WPI; 1991-016179/03.		CC	Nucleic acid comprising a sequence encoding amino acids 14-414 of	
XX	N-PSDB; AAQ10230.		CC	streptokinase, which binds to plasminogen and does not have a sequence	
PT	Synthetic gene encoding streptokinase - scale, high purity prodn. of		CC	comprising amino acids 60-414 is new. The polypeptide pref. comprises	
PT	streptokinase used as a thrombolytic agent.		CC	amino acids 244-352, 1-352, 120-352 or 244-414. (Updated on 25-MAR-2003	
XX	Claim 1; Page 51; 76PP; English.		CC	to correct PN field.) (Updated on 16-OCT-2003 to standardise OS field)	
PS			XX		
XX			SQ	Sequence 414 AA;	
CC	Streptokinase and its derivatives can be produced in large quantities		Query Match	5.0%; Score 31.5; DB 2; Length 414;	
CC	with high purity for use as thrombolytic agents in patients with lung		Best Local Similarity	5.0%; Score 31.5; DB 2; Length 414;	
CC	thrombus or myocardial infarction. See also AAR10195-R10200		Matches	32.0%; Pred. No. 7.6;	
XX	Sequence 414 AA;		XX	Matches 16; Conservative 8; Mismatches 8; Gaps 3;	
SQ			XX	Indels 17; Gaps 3;	
Qy	203	QDTR-TSYRIGDTWSKKDKNRGNL---QCICITGNGRGEWKCRERTSVQT 247	RESULT 5	AAW94664	
Db	180	KDTKLKTLAIGTRITRQ-----LLAQAGSILANKNHPGTYIERTDSSITV 225	ID	AAW94664 standard; protein; 414 AA.	
AC			XX	AAW94664;	
XX			AC		
AAR63120			XX		
ID	AAR63120	standard; protein; 414 AA.	DT	17-OCT-2003 (revised)	
XX			XX	Streptococcus equisimilis native streptokinase.	
DT	16-OCT-2003 (revised)		DT	04-MAY-1999 (first entry)	
DT	25-MAR-2003 (revised)		KW	Streptococcus equisimilis H46A; streptokinase; mutant; fibrinolytic;	
			KW	plasminogen; plasmin; plasminogen; plasmin;	

KW	serine protease; fibrin; blood clot; thrombolytic;	PD	25-FEB-1999.
KW	vascular thromboembolic symptom; acute myocardial infarction.	XX	18-AUG-1998;
KW	fibrinolysis; resistance.	PF	98WO-US017114.
XX		PR	18-AUG-1997;
OS	Streptococcus dysgalactiae subsp. equisimilis.	XX	97US-0055911P.
XX		PA	(HARD ) HARVARD COLLEGE.
XX	Location/Qualifiers	PA	GEN HOSPITAL CORP.
FH		XX	
FT	Key-Misc-difference 14	PI	Reed GL, Parhami-Seran B;
FT	/note= "encoded by ACC"	XX	
XX		DR	WPI; 1999-130113/16.
PN	US5876999-A.	PS	PS Disclosure; Page 12; 44pp; English.
XX		XX	
XX	02-MAR-1999.	PS	New polypeptides which bind streptokinase-specific antibodies - useful in thrombolytic therapy.
XX		PR	PR Disclosure; Page 12; 44pp; English.
XX	06-DEC-1995;	XX	
PF	95US-00568393.	PS	The present sequence represents a native streptokinase. The specification describes a polypeptide which binds to a streptokinase-specific antibody and prevents the antibody binding to native streptokinase. The specification also describes a synthetic polypeptide (P1) comprising an epitope which binds to an streptokinase-specific antibody and reduces thrombolytic activity of streptokinase. P1 is used in thrombolytic therapy, and to prevent or treat glomerulonephritis and rheumatic fever.
XX		CC	(Updated on 17-OCT-2003 to standardise OS field)
PR	06-DEC-1995;	XX	
XX	95US-00568393.	PS	PS Disclosure; Page 12; 44pp; English.
XX		XX	
XX	(NASC-) NAT SCI COUNCIL.	CC	The present invention describes a mutant streptokinase (SK) polypeptide in which at least one of the amino acids in the Pro58-Lys59-Ser60-Lys61 segment of the corresponding native SK is replaced by another amino acid.
XX		CC	The present sequence represents native SK. SK is a secretory protein of haemolytic Streptococcus able to activate human plasminogen (HPlg) to plasmin (HPlm), which is a serine protease able to catalyse the hydrolysis of fibrin in blood clots. The SK is useful as a thrombolytic agent in the treatment of vascular thromboembolic symptoms such as acute myocardial infarction. Compared with wild-type SK, the K59E mutant is more resistant to degradation by human plasmin and is more effective both in acting as a fibrolytic agent and in activating human plasminogen.
PI	Wu H;	CC	(Updated on 17-OCT-2003 to standardise OS field)
XX		CC	
XX	WPI; 1999-189643/16.	CC	RESULT 7
DR	-N-PSDB; AAX16632.	CC	AY24794
XX		CC	AY24794 standard; protein; 414 AA.
PT	Mutant streptokinase polypeptide - useful as plasmin-resistant thrombolytic agent.	XX	
XX		AC	AY24794;
PS	Claim 1; Col 7-10; 17pp; English.	AC	Sequence 414 AA;
XX		XX	XX
CC	The present invention describes a mutant streptokinase (SK) polypeptide in which at least one of the amino acids in the Pro58-Lys59-Ser60-Lys61 segment of the corresponding native SK is replaced by another amino acid.	Query	Query Match Score 5.0%; Best Local Similarity 32.0%; Matches 16; Conservative 8; Mismatches 8; Gaps 3;
CC	The present sequence represents native SK. SK is a secretory protein of haemolytic Streptococcus able to activate human plasminogen (HPlg) to plasmin (HPlm), which is a serine protease able to catalyse the hydrolysis of fibrin in blood clots. The SK is useful as a thrombolytic agent in the treatment of vascular thromboembolic symptoms such as acute myocardial infarction. Compared with wild-type SK, the K59E mutant is more resistant to degradation by human plasmin and is more effective both in acting as a fibrolytic agent and in activating human plasminogen.	Db	203 QDTR--TSDRIGDTWSKCDNQRNLL--QCICITGNNGRGEWKCRHRTSVQT 247 180 KDTKLKLTIAIGDTITSQE---LLAQOSILNKNHPGTYIERTDSSIVT 225
CC	(Updated on 17-OCT-2003 to standardise OS field)	XX	XX
XX		XX	XX
XX	Sequence 414 AA;	XX	XX
PS		DT	17-OCT-2003 (revised)
XX		DT	26-AUG-1999 (first entry)
CC		XX	Streptococcus equisimilis native streptokinase.
CC		DE	
CC		XX	Streptococcus; streptokinase; fibrin-dependent plasminogen activator; nsk; rsk; bacterial; blood clot; thrombotic condition;
CC		XX	KW myocardial infarction; venous thrombosis; pulmonary embolism; cerebral thrombosis; graft thrombosis; arterial thrombosis.
CC		XX	OS Streptococcus dysgalactiae subsp. equisimilis.
CC		XX	PN W09931247-A1.
CC		XX	XX
AC	AY01556	PD	24-JUN-1999.
XX		XX	
DT	17-OCT-2003 (revised)	PF	15-DEC-1998; 98WO-US026694.
DT	18-JUN-1999 (first entry)	PR	15-DEC-1997; 97US-0069497P.
XX		PA	(HARD ) HARVARD COLLEGE.
DE	Native streptokinase protein sequence.	XX	
XX		PI	Reed GL;
KW	Antigenic peptide; Streptokinase; streptokinase-specific antibody; thromolytic activity; thrombolytic therapy; glomerulonephritis; rheumatic fever.	XX	DR WPI; 1999-395183/33.
KW	Streptococcus dysgalactiae subsp. equisimilis.	XX	DR N-PSDB; AAXB0492.
KW		PT	N-terminally deleted streptokinase.
XX		XX	
OS	W09908698-A1.	XX	
XX		XX	



